******* QUERY RESULTS *******

```
=> d his l33

     (FILE 'HCAPLUS' ENTERED AT 14:40:20 ON 24 MAY 2007)
L33          24 S L32 OR L24

=> d que l33
L4            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  145375-43-5/RN
L5            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  207844-01-7/RN
L6            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  MITIGLINIDE/CN
L8            2 SEA FILE=REGISTRY ABB=ON  PLU=ON  (L4 OR L5 OR L6)
L9           97 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8 OR MITIGLINIDE CALCIUM
                 HYDRATE/OBI
L10          87 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MITIGLINIDE/OBI OR MITI/OBI(W)
                 GLINIDE/OBI
L11         108 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 OR L10
L13     2160940 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (INHIBIT?/OBI OR HINDER?/OBI
                 OR IMPED?/OBI OR REDUC?/OBI OR REDN#/OBI OR SUPPRESS?/OBI OR
                 PREVENT?/OBI OR BLOCK?/OBI OR ELIMINAT?/OBI)
L19      110617 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DIABET?/OBI
L20          54 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11 AND L19
L22          28 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L13 (5A) L20
L23             QUE  ABB=ON  PLU=ON  AY<2004 OR PRY<2004 OR PY<2004 OR MY
                 <2004 OR REVIEW/DT
L24          17 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L22 AND L23
L27         271 SEA FILE=HCAPLUS ABB=ON  PLU=ON  HYPERGLYCEM?/OBI (3A)
                 (POST/OBI(W)PRANDIAL/OBI OR POSTPRANDIAL/OBI)
L28           3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11 AND L27
L29       13237 SEA FILE=HCAPLUS ABB=ON  PLU=ON  HYPERGLYCEM?/OBI
L30       13237 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L27 OR L29
L31           7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11 AND L30
L32           7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L28 OR L31
L33          24 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L32 OR L24


=> d his l49

     (FILE 'MEDLINE, BIOSIS, EMBASE, DRUGU' ENTERED AT 14:54:53 ON 24 MAY 2007)
L49          33 S L48 (P) L13

=> d que l49
L4            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  145375-43-5/RN
L5            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  207844-01-7/RN
L6            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  MITIGLINIDE/CN
L8            2 SEA FILE=REGISTRY ABB=ON  PLU=ON  (L4 OR L5 OR L6)
L10          87 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MITIGLINIDE/OBI OR MITI/OBI(W)
                 GLINIDE/OBI
L13     2160940 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (INHIBIT?/OBI OR HINDER?/OBI
                 OR IMPED?/OBI OR REDUC?/OBI OR REDN#/OBI OR SUPPRESS?/OBI OR
                 PREVENT?/OBI OR BLOCK?/OBI OR ELIMINAT?/OBI)
L19      110617 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DIABET?/OBI
L23             QUE  ABB=ON  PLU=ON  AY<2004 OR PRY<2004 OR PY<2004 OR MY
                 <2004 OR REVIEW/DT
L27         271 SEA FILE=HCAPLUS ABB=ON  PLU=ON  HYPERGLYCEM?/OBI (3A)
                 (POST/OBI(W)PRANDIAL/OBI OR POSTPRANDIAL/OBI)
L29       13237 SEA FILE=HCAPLUS ABB=ON  PLU=ON  HYPERGLYCEM?/OBI
L43          84 SEA L8
L44         172 SEA L10
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L45          10 SEA MITIGLINIDE CALCIUM HYDRATE
L46         173 SEA (L43 OR L44 OR L45)
L47         110 SEA L46 AND (L19 OR L27 OR L29)
L48          46 SEA L47 AND L23
L49          33 SEA L48 (P) L13


=> dup rem l33 l49
FILE 'HCAPLUS' ENTERED AT 15:07:58 ON 24 MAY 2007
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FILE 'DRUGU' ENTERED AT 15:07:58 ON 24 MAY 2007
COPYRIGHT (C) 2007 THE THOMSON CORPORATION
PROCESSING COMPLETED FOR L33
PROCESSING COMPLETED FOR L49
L61          49 DUP REM L33 L49 (8 DUPLICATES REMOVED)
                ANSWERS '1-24' FROM FILE HCAPLUS
                ANSWERS '25-42' FROM FILE MEDLINE
                ANSWERS '43-45' FROM FILE EMBASE
                ANSWERS '46-49' FROM FILE DRUGU

=> d l61 1-24 ibib ed abs hitind

L61  ANSWER 1 OF 49  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2006:505268  HCAPLUS  Full-text
DOCUMENT NUMBER:          145:483552
TITLE:                    Therapeutic efficacy of mitiglinide combined
                          with once daily insulin glargine after switching from
                          multiple daily insulin regimen of aspart insulin and
                          glargine in patients with type 2 diabetes mellitus
AUTHOR(S):                Yoshihara, Tomoaki; Kumashiro, Naoki; Kanazawa,
                          Yoshie; Mita, Tomoya; Sakurai, Yuko; Kawai, Junko;
                          Abe, Michiko; Motojima, Kayoko; Hara, Kanako;
                          Yamazaki, Yuka; Kanazawa, Akio; Miwa, Shinya; Sato,
                          Fumihiko; Kanno, Rei; Shimizu, Tomoaki; Sakai, Ken;
                          Uchino, Hiroshi; Watada, Hirotaka; Tanaka, Yasushi;
                          Kawamori, Ryuzo; Hirose, Takahisa
CORPORATE SOURCE:          Department of Medicine, Metabolism and Endocrinology,
                          School of Medicine, Juntendo University, Bunkyo-ku,
                          Tokyo, 113-8421, Japan
SOURCE:                   Endocrine Journal (Kyoto, Japan) (2006), 53(1), 67-72
                          CODEN: ENJOEO; ISSN: 0918-8959
PUBLISHER:                Japan Endocrine Society
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
ED   Entered STN:  31 May 2006
AB   Mitiglinide is novel class of rapid-acting insulin secretagogues, which have
     been widely used alone or in combination with other oral hypoglycemic drugs to
     improve postprandial hyperglycemia in early type 2 diabetes. While mitiglinide
     enhances postprandial requirement of insulin, the efficacy of mitiglinide
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combined with insulin has yet to be established. We investigated the efficacy of mitiglinide combined with insulin glargine, the first soluble insulin analog that has a flat and prolonged effect. After control with the intensive regimen (daily aspart insulin and glargine), 30 inpatients with type 2 diabetes were switched to premeal mitiglinide combined with once daily insulin glargine (mitiglinide regimen), and daily profiles of blood glucose level were compared under each regimen. Fifteen patients showed similar control of hyperglycemia with mitiglinide regimen and intensive insulin regimen, assessed by M value (<32), while the remaining 15 showed worsening under the mitiglinide regimen. The patients who were well controlled with mitiglinide regimen were significantly younger (51.9 ± 16.0 years, $p<0.005$) and heavier (body mass index: 25.7 ± 3.3 kg/m2, $p<0.05$) than those who were not (67.9 ± 8.7 and 23.0 ± 3.1, resp.). Moreover, insulin doses of aspart per body weight were significantly fewer in effective group than in ineffective group. Duration of diabetes was shorter in the effective group, albeit insignificantly. Previous treatment before starting intensive insulin regimen, such as insulin and sulfonylurea, was not different between the two groups. Our results suggest that mitiglinide plus insulin glargine combination therapy is useful for lowering both fasting and postprandial hyperglycemia in a subpopulation of type 2 diabetes. The long-term effects of such treatment need to be established in future studies.

CC 1-10 (Pharmacology)

ST **mitiglinide** insulin glargine **hyperglycemia** type2 diabetes mellitus antidiabetic

IT Antidiabetic agents
Body weight
Combination chemotherapy
Human
Hyperglycemia
(**mitiglinide** combined with once daily insulin glargine after switching from multiple daily insulin regimen of aspart insulin and glargine lowered both fasting and **postprandial** **hyperglycemia** in patient with type 2 diabetes mellitus)

IT Glycerides, biological studies
High-density lipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**mitiglinide** combined with once daily insulin glargine after switching from multiple daily insulin regimen of aspart insulin and glargine lowered both fasting and **postprandial** **hyperglycemia** in patient with type 2 diabetes mellitus)

IT Diabetes mellitus
(non-insulin-dependent; **mitiglinide** combined with once daily insulin glargine after switching from multiple daily insulin regimen of aspart insulin and glargine lowered both fasting and **postprandial hyperglycemia** in patient with type 2 diabetes mellitus)

IT 50-99-7, D-Glucose, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(blood; **mitiglinide** combined with once daily insulin glargine after switching from multiple daily insulin regimen of aspart insulin and glargine lowered both fasting and **postprandial** **hyperglycemia** in patient with type 2 diabetes mellitus)

IT 57-88-5, Cholesterol, biological studies 62572-11-6, Hemoglobin A1c
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**mitiglinide** combined with once daily insulin glargine after switching from multiple daily insulin regimen of aspart insulin and glargine lowered both fasting and **postprandial** **hyperglycemia** in patient with type 2 diabetes mellitus)

IT 9004-10-8, Insulin, biological studies **145375-43-5**, **Mitiglinide** 160337-95-1

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**mitiglinide** combined with once daily insulin glargine after switching from multiple daily insulin regimen of aspart insulin and glargine lowered both fasting and **postprandial hyperglycemia** in patient with type 2 diabetes mellitus)
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 2 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:962511 HCAPLUS Full-text
DOCUMENT NUMBER: 143:244659
TITLE: Method for examining blood glucose control state
INVENTOR(S): Kitahara, Yoshiro; Miura, Kyoko; Takeuchi, Masayoshi
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005080993	A1	20050901	WO 2005-JP3438	20050223

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

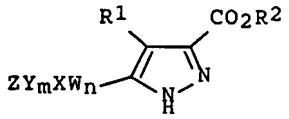
PRIORITY APPLN. INFO.: JP 2004-47020 A 20040223
ED Entered STN: 02 Sep 2005
AB A novel diagnostic marker for a blood glucose control state is provided. Also provided is a method for diagnosing or examining a blood glucose control state. The method comprises a process for measuring the AGE2 concentration in a blood or body fluid sample of a patient by a measuring method selected from a Western blotting method, an enzyme immunoassay, a RIA, a liquid chromatog. and a dot blot method, and a process for evaluating the state of postprandial hyperglycemia control.
IC ICM G01N033-68
ICS G01N033-15; G01N033-50; G01N033-53; G01N033-577; G01N033-66
CC 9-10 (Biochemical Methods)
Section cross-reference(s): 14
IT **Hyperglycemia**
(**postprandial**; method for examining blood glucose control state by measuring blood AGE2)
IT 54870-28-9D, Meglitinide, derivative 105816-04-4, Nateglinide 135062-02-1, Repaglinide **145375-43-5, Mitiglinide**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for examining blood glucose control state by measuring blood AGE2)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 3 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:120729 HCAPLUS Full-text
DOCUMENT NUMBER: 142:219276
TITLE: Preparation of 5-substituted 2H-pyrazole-3-carboxylic acid derivatives as agonists for the RUP25 nicotinic acid receptor for the treatment of dyslipidemia and related diseases
INVENTOR(S): Semple, Graeme; Gharbaoui, Tawfik; Shin, Young-Jun; Decaire, Marc; Averbuj, Claudia; Skinner, Philip J.
PATENT ASSIGNEE(S): Arena Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005011677	A1	20050210	WO 2004-US18389	20040610 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004260636	A1	20050210	AU 2004-260636	20040610 <--
CA 2528834	A1	20050210	CA 2004-2528834	20040610 <--
EP 1633351	A1	20060315	EP 2004-776418	20040610 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 2007032537	A1	20070208	US 2006-560332	20060908 <--
PRIORITY APPLN. INFO.:			US 2003-478664P	P 20030613 <--
			WO 2004-US18389	W 20040610

OTHER SOURCE(S): MARPAT 142:219276
ED Entered STN: 11 Feb 2005
GI



I

AB Title compds. [I; W, Y = (substituted) alkylene, alkenylene, alkynylene; X = NR3CO, NR3SO2, NR3, CO, CH(OH), C(NH), O, S, SO, SO2, etc.; R3, R4 = H, (substituted) alkyl, Ph, heteroaryl; Z = H, halo, (substituted) Ph, heteroaryl; R1 = H, OH, halo, alkyl, haloalkyl; R2 = H, alkyl; m, n = 0, 1; with provisos], were prepared Thus, 5-methylthiomethyl-2H-pyrazole-3-carboxylic acid (preparation outlined) showed hRUP25 agonist activity with EC50 = 4.3 μM.

IC ICM A61K031-415
ICS C07D231-14; A61P003-06
CC 28-8 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
ST pyrazolecarboxylate prepn RUP25 nicotinic acid receptor agonist; dyslipidemia atherosclerosis heart disease **diabetes** obesity treatment pyrazolecarboxylate prepn
IT **Diabetes** mellitus
(non-insulin-dependent, treatment; preparation of pyrazolecarboxylates as agonists for the RUP25 nicotinic acid receptor for the treatment of dyslipidemia and related diseases)
IT 64-77-7, Tolbutamide 94-20-2, Chlorpropamide 114-86-3, Phenformin 339-43-5, Carbutamide 339-44-6, Glymidine 451-71-8, Glyhexamide 535-65-9, Glybuthiazole 631-27-6, Glyclopyramide 637-07-0, Clofibrate 657-24-9, Metformin 664-95-9, Tolcyclamide 692-13-7, Buformin 882-09-7, Clofibric acid 968-81-0, Acetohexamide 1156-19-0, Tolazamide 1228-19-9, Glypinamide 1492-02-0, Glybuzole 3149-00-6, Phenbutamide 3459-20-9, Glymidine 4618-41-1, 1-Butyl-3-metanilylurea 10238-21-8, Glibenclamide 14929-11-4, Simfibrate 21187-98-4, Gliclazide 25046-79-1, Glisoxepid 25812-30-0, Gemfibrozil 26944-48-9, Glibornuride 29094-61-9, Glipizide 30299-08-2, Clinofibrate 31637-97-5, Etofibrate 31980-29-7, Nicofibrate 33342-05-1, Gliquidone 41859-67-0, Bezafibrate 42597-57-9, Ronifibrate, biological studies 49562-28-9, Fenofibrate 52214-84-3, Ciprofibrate 54504-70-0, Theofibrate 55285-45-5, Pirifibrate 55937-99-0, Beclobrate 56180-94-0, Acarbose 62571-86-2, Captopril 68367-52-2, Sorbinil 69047-39-8, Binifibrate 72432-03-2, Miglitol 74258-86-9, Alacepril 75330-75-5, Lovastatin 75847-73-3, Enalapril 76420-72-9, Enalaprilat 76547-98-3, Lisinopril 79902-63-9, Simvastatin 81093-37-0, Pravastatin 82159-09-9, Epalrestat 82834-16-0, Perindopril 82964-04-3, Tolrestat 83435-66-9, Delapril 83480-29-9, Voglibose 83647-97-6, Spirapril 85441-61-8, Quinapril 85856-54-8, Moveltipril 86541-75-5, Benazepril 87333-19-5, Ramipril 87679-37-6, Trandolapril 88768-40-5, Cilazapril 89371-37-9, Imidapril 89391-50-4, Imirestat 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 98048-97-6, Fosinopril 105816-04-4, Nateglinide 110703-94-1, Zopolrestat 111025-46-8, Pioglitazone 111223-26-8, Ceronapril 111902-57-9, Temocapril 112733-06-9, Zenarestat 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin **145375-43-5**, **Mitiglinide** 145599-86-6, Cerivastatin 287714-41-4, Rosuvastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of pyrazolecarboxylates as agonists for the RUP25 nicotinic acid receptor for the treatment of dyslipidemia and related diseases)
IT 9001-42-7, α-Glucosidase 9028-31-3, Aldose **reductase** 9028-35-7, Hmg coa **reductase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors** coadministration; preparation of pyrazolecarboxylates as agonists for the RUP25 nicotinic acid receptor for the treatment of dyslipidemia and related diseases)
IT 9015-82-1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**, coadministration; preparation of pyrazolecarboxylates as agonists for the RUP25 nicotinic acid receptor for the treatment of dyslipidemia and related diseases)
IT 111-02-4, Squalene
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(synthesis **inhibitors** coadministration; preparation of pyrazolecarboxylates as agonists for the RUP25 nicotinic acid receptor for the treatment of dyslipidemia and related diseases)

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 4 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1009580 HCAPLUS Full-text
DOCUMENT NUMBER: 144:142642
TITLE: Effects of S21403 (**mitiglinide**) on postprandial generation of oxidative stress and inflammation in type 2 diabetic patients
AUTHOR(S): Assaloni, R.; Ros, R. Da; Quagliaro, L.; Piconi, L.; Maier, A.; Zuodar, G.; Motz, E.; Ceriello, A.
CORPORATE SOURCE: Department of Pathology and Medicine, Experimental and Clinical, University of Udine, Udine, Italy
SOURCE: Diabetologia (2005), 48(9), 1919-1924
CODEN: DBTGAJ; ISSN: 0012-186X
PUBLISHER: Springer GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 19 Sep 2005
AB Aim/hypothesis: Evidence suggests that postprandial hyperglycemia may be a cardiovascular risk factor in diabetes. Oxidative stress and inflammation are involved in the pathogenesis of diabetic complications and previous studies have shown increased oxidative stress and inflammation in the postprandial phase in diabetic patients. The aim of the present study was to evaluate whether controlling postprandial hyperglycemia with S21403 (mitiglinide) is accompanied by a reduced generation of oxidative stress and inflammation. Subjects and methods: Forty type 2 diabetic patients participated in the study. Two different breakfast-tests were performed in each patient, with placebo or S21403. Plasma nitrotyrosine, plasma malondialdehyde (MDA), oxidized LDL (oxLDL), plasma total radical-trapping antioxidant parameter (TRAP), IL-6, IL-18, TNF-α, plasma glucose and insulin were measured. Results: After the administration of S21403, 40 mg, a rapid stimulation of insulin secretion was observed, accompanied by a reduction of postprandial hyperglycemia. With S21403, a significant decrease of either nitrotyrosine, MDA and oxLDL levels, and a preservation of plasma TRAP compared with placebo was found. Significant decreases of IL-6, IL-18 and TNF-α were also observed with S21403 compared with placebo. Conclusions/interpretation: This study shows that controlling postprandial hyperglycemia with S21403 significantly improves the cluster of oxidative stress and inflammation markers that are increased in the postprandial state in diabetic patients.
CC 1-10 (Pharmacology)
ST **mitiglinide postprandial hyperglycemia** oxidative stress inflammation diabetes antidiabetic
IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study) (SSR (signal sequence receptor); controlling **postprandial hyperglycemia** with S21403 significantly decreased oxidative stress markers nitrotyrosine, MDA, oxLDL levels and preserved plasma TRAP in type 2 diabetic patient)
IT Interleukin 18
RL: BSU (Biological study, unclassified); BIOL (Biological study) (controlling **postprandial hyperglycemia** with S21403 significantly decreased inflammatory marker interleukin-18 in type 2 diabetic patient)
IT Interleukin 6
RL: BSU (Biological study, unclassified); BIOL (Biological study) (controlling **postprandial hyperglycemia** with S21403 significantly decreased inflammatory marker interleukin-6 in type 2 diabetic patient)
IT Tumor necrosis factors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(controlling **postprandial hyperglycemia** with S21403 significantly decreased inflammatory marker tumor necrosis factor-α in type 2 diabetic patient)

IT Inflammation
(controlling **postprandial hyperglycemia** with S21403 significantly decreased inflammatory markers IL-6, IL-18, TNF-α in type 2 diabetic patient)

IT Human
Hyperglycemia
Pancreas
(controlling **postprandial hyperglycemia** with S21403 significantly decreased oxidative stress markers nitrotyrosine, MDA, oxLDL levels, inflammatory markers IL-6, IL-18, TNF-α and preserved plasma TRAP in type 2 diabetic patient)

IT Oxidative stress, biological
(controlling **postprandial hyperglycemia** with S21403 significantly decreased oxidative stress markers nitrotyrosine, malondialdehyde, oxLDL levels and preserved plasma TRAP in type 2 diabetic patient)

IT Antidiabetic agents
(controlling **postprandial hyperglycemia** with **mitiglinide** significantly decreased oxidative stress markers nitrotyrosine, MDA, oxLDL levels, inflammatory markers IL-6, IL-18, TNF-α and preserved plasma TRAP in type 2 diabetic patient)

IT Diabetes mellitus
(non-insulin-dependent; controlling **postprandial hyperglycemia** with S21403 significantly decreased oxidative stress markers nitrotyrosine, MDA, oxLDL levels, inflammatory markers IL-6, IL-18, TNF-α and preserved plasma TRAP in type 2 diabetic patient)

IT Low-density lipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(oxidized; controlling **postprandial hyperglycemia** with S21403 significantly decreased oxidative stress marker oxLDL levels in type 2 diabetic patient)

IT 50-99-7, Glucose, biological studies 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(S21403 stimulated insulin secretion which was accompanied by reduction of **postprandial hyperglycemia** in type 2 diabetic patient)

IT 542-78-9, Malondialdehyde
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(controlling **postprandial hyperglycemia** with S21403 significantly decreased oxidative stress marker malondialdehyde in type 2 diabetic patient)

IT 621-44-3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(controlling **postprandial hyperglycemia** with S21403 significantly decreased oxidative stress marker nitrotyrosine in type 2 diabetic patient)

IT **145375-43-5, Mitiglinide**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlling **postprandial hyperglycemia** with **mitiglinide** significantly decreased oxidative stress markers nitrotyrosine, MDA, oxLDL levels, inflammatory markers IL-6, IL-18, TNF-α and preserved plasma TRAP in type 2 diabetic patient)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 5 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:902180 HCAPLUS Full-text
DOCUMENT NUMBER: 141:355415
TITLE: A synergistic pharmaceutical combination comprising cicletanine for the prevention or treatment of diabetes
INVENTOR(S): Egri, Janos
PATENT ASSIGNEE(S): Synosens Kutato es Fejleszto Kft., Hung.
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004091612	A1	20041028	WO 2004-HU37		20040414 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
HU 200300990	A2	20050530	HU 2003-990		20030415 <--
CA 2522126	A1	20041028	CA 2004-2522126		20040414 <--
EP 1648453	A1	20060426	EP 2004-727331		20040414 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK					
JP 2006523668	T	20061019	JP 2006-506248		20040414 <--
PRIORITY APPLN. INFO.:			HU 2003-990	A	20030415 <--
			WO 2004-HU37	W	20040414

OTHER SOURCE(S): MARPAT 141:355415
ED Entered STN: 28 Oct 2004
AB The invention refers to a synergistic pharmaceutical combination comprising (a) a first pharmaceutical composition containing cicletanine or a pharmaceutically suitable acid addition salt thereof and one or more conventional carrier(s), and (b) a second pharmaceutical composition containing an antidiabetic or antihyperlipidemic active agent or, if desired and chemical possible, a pharmaceutically suitable acid addition salt or a salt formed with a pharmaceutically suitable base thereof and one or more conventional carrier(s). An antidiabetic agent is selected from a thiazolidinedione derivative, a sulfonylurea, or a biguanidine derivative The pharmaceutical combination is suitable for the prevention or treatment of a prediabetic state, metabolic X-syndrome or diabetes mellitus, as well as disorders associated with these states.
IC ICM A61K031-4355
ICS A61K031-155; A61K031-427; A61K031-64; A61P003-00; A61P003-10
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 2
ST cicletanine antidiabetic hypolipemic synergy diabetes complication

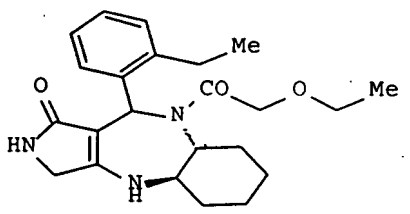
IT Hair, disease
(diffuse effluvium; synergistic combination comprising cicletanine for **prevention** or treatment of **diabetes** and related disorders)
IT Metabolic disorders
(metabolic syndrome X; synergistic combination comprising cicletanine for **prevention** or treatment of **diabetes** and related disorders)
IT Antidiabetic agents
(oral; synergistic combination comprising cicletanine for **prevention** or treatment of **diabetes** and related disorders)
IT Ovary, disease
(polycystic; synergistic combination comprising cicletanine for **prevention** or treatment of **diabetes** and related disorders)
IT Alopecia
Antidiabetic agents
Combination chemotherapy
Diabetes mellitus
Hypolipemic agents
(synergistic combination comprising cicletanine for **prevention** or treatment of **diabetes** and related disorders)
IT Dyslipidemia
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(synergistic combination comprising cicletanine for **prevention** or treatment of **diabetes** and related disorders)
IT Sulfonylureas
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synergistic combination comprising cicletanine for **prevention** or treatment of **diabetes** and related disorders)
IT Drug interactions
(synergistic; synergistic combination comprising cicletanine for **prevention** or treatment of **diabetes** and related disorders)
IT 10238-21-8, Glyburide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Glibenclamide; synergistic combination comprising cicletanine for **prevention** or treatment of **diabetes** and related disorders)
IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(resistance; synergistic combination comprising cicletanine for **prevention** or treatment of **diabetes** and related disorders)
IT 64-77-7, Tolbutamide 94-20-2, Chloropropamide 114-86-3, Phenformin 631-27-6, Glyclopyramide 637-07-0, Clofibrate 657-24-9, Metformin 692-13-7, Buformin 968-81-0, Acetohexamide 1156-19-0, Tolazamide 1492-02-0, Glybuzole 2295-31-0D, Thiazolidinedione, derivs. 5868-05-3, Niceritrol 6882-47-9D, Biguanidine, derivs. 10571-59-2, Nicoclonate 11041-12-6, Cholestyramine 14929-11-4, Simfibrate 21187-98-4, Gliclazide 24477-37-0, Glisolamide 25046-79-1, Glisoxepid 25812-30-0, Gemfibrozil 26944-48-9, Glibornuride 27959-26-8, Nicomol 29094-61-9, Glipizide 31637-97-5, Etofibrate 32797-92-5, Glisentide 33342-05-1, Gliquidone 42597-57-9, Ronifibrate, biological studies 50925-79-6, Colestipol 51037-30-0, Acipimox 52214-84-3, Ciprofibrate 56180-94-0, Acarbose 56227-39-5, Polidexide 72432-03-2, Miglitol 74772-77-3, Ciglitazone 75330-75-5, Lovastatin 79902-63-9, Simvastatin 81093-37-0, Pravastatin 82747-56-6, Cicletanine hydrochloride

83480-29-9, Voglibose 89943-82-8, Cicletanine 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 97322-87-7, Troglitazone 105816-04-4, Senaglinide 111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1, Repaglinide **145375-43-5**, **Mitiglinide**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synergistic combination comprising cicletanine for **prevention** or treatment of **diabetes** and related disorders)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 6 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:681582 HCAPLUS Full-text
DOCUMENT NUMBER: 141:185111
TITLE: Remedy for **diabetes**
INVENTOR(S): Ikenoue, Takao; Kageyama, Yoko; Iino, Yukio; Kondo, Nobuo
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004069259	A1	20040819	WO 2004-JP1279	20040206 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004210268	A1	20040819	AU 2004-210268	20040206 <--
CA 2515294	A1	20040819	CA 2004-2515294	20040206 <--
EP 1595544	A1	20051116	EP 2004-708897	20040206 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2004007303	A	20060207	BR 2004-7303	20040206 <--
CN 1771040	A	20060510	CN 2004-80009410	20040206 <--
US 2005272641	A1	20051208	US 2005-198511	20050808 <--
PRIORITY APPLN. INFO.:			JP 2003-31088 A	20030207 <--
			WO 2004-JP1279 A	20040206

OTHER SOURCE(S): MARPAT 141:185111
ED Entered STN: 20 Aug 2004
GI



I

AB A preventive and/or a remedy for diabetes, diabetic complications, hyperinsulinemia, sugar metabolic error or obesity characterized by comprising a combination of a compound represented by the following formula (I; Markush's structures given), its analog or a pharmaceutically acceptable salt thereof with a hypoglycemic agent.

IC ICM A61K031-5517
ICS A61K031-551; A61K031-553; A61K031-554; A61P003-04; A61P003-10; A61P043-00; A61K045-00; C07D487-04

CC 1-10 (Pharmacology)
Section cross-reference(s): 2

IT Nerve, disease
(**diabetic** neuropathy; heterocyclic compds. as antidiabetic and antiobesity agents)

IT Antidiabetic agents
Antihypertensives
Antiobesity agents
Antioxidants
Diabetes mellitus
Drug resistance
Obesity
β3-Adrenoceptor agonists
(heterocyclic compds. as antidiabetic and antiobesity agents)

IT 56-03-1D, Biguanide, derivs. 114-86-3, Fenformin 657-24-9, Metformin 692-13-7, Buformin 10238-21-8, Glibenclamide 21187-98-4, Gliclazide 56180-94-0, Acarbose 105816-04-4, Nateglinide 111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone **145375-43-5**, **Mitiglinide** 433729-78-3 433729-79-4 433729-80-7 433729-81-8 433729-82-9 433729-83-0 433729-84-1 433729-85-2 433729-86-3 433729-87-4 433729-88-5 433729-89-6 433729-90-9 433729-91-0 433729-92-1 433729-93-2 433729-94-3 433729-95-4 433729-96-5 433729-97-6 433729-98-7 433729-99-8 433730-00-8 433730-01-9 433730-02-0 433730-03-1 433730-04-2 433730-05-3 433730-06-4 433730-07-5 433730-08-6 433730-09-7 433730-10-0 433730-11-1 433730-12-2 433730-13-3 433730-14-4 433730-15-5 433730-16-6 433730-17-7 433730-18-8 433730-19-9 433730-20-2 433730-21-3 433730-22-4 433730-23-5 433730-24-6 433730-25-7 433730-26-8 433730-27-9 433730-28-0 433730-29-1 433730-30-4 433730-31-5 433730-32-6 433730-33-7 433730-34-8 433730-35-9 433730-36-0 433730-37-1 433730-38-2 433730-39-3 433730-40-6 433730-41-7 433730-42-8 433730-43-9 433730-44-0 433730-45-1 433730-46-2 433730-47-3 433730-48-4 433730-49-5 433730-50-8 433730-51-9 433730-52-0 433730-53-1 433730-54-2 433730-55-3 433730-56-4 433730-57-5 433730-58-6 433730-59-7 433730-60-0 433730-61-1 433730-62-2 433730-63-3 433730-64-4 433730-65-5 433730-66-6 433730-67-7 433730-68-8 433730-69-9 433730-70-2 433730-72-4 433730-73-5 433730-75-7 433730-76-8 433730-77-9 433730-78-0 433730-79-1 433730-80-4 433730-81-5 433730-82-6 433730-83-7 433730-84-8 433730-85-9 433730-86-0 433730-87-1 433730-88-2 433730-89-3 433730-90-6 433730-91-7 433730-92-8 433730-93-9 433730-94-0 433730-95-1 433730-96-2 433730-97-3 433730-98-4 433730-99-5 433731-00-1 433731-01-2 433731-02-3 433731-04-5 433731-06-7 433731-08-9 433731-09-0 433731-10-3 433731-11-4 737804-07-8 737804-08-9 737804-09-0 737804-10-3 737804-11-4 737804-12-5 737804-13-6 737804-14-7 737804-15-8 737804-16-9 737804-17-0 737804-18-1 737804-19-2 737804-20-5 737804-21-6 737804-22-7 737804-23-8 737804-24-9 737804-25-0

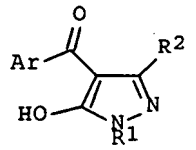
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heterocyclic compds. as antidiabetic and antiobesity agents)

IT 9001-62-1, Lipase 9028-31-3, Aldose **reductase** 9035-74-9, Glycogen phosphorylase 54249-88-6, Dipeptidyl peptidase IV
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; heterocyclic compds. as antidiabetic and antiobesity agents)

L61 ANSWER 7 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:333698 HCAPLUS Full-text
DOCUMENT NUMBER: 140:357333
TITLE: Preparation of aroylhydroxypyrazoles for treatment of metabolic disorders
INVENTOR(S): Semple, Graeme; Shin, Young Jun
PATENT ASSIGNEE(S): Arena Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 2004033431	A2	20040422	WO 2003-US31509		20031002	<--
WO 2004033431	A3	20040729				
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW						
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG						
AU 2003282679	A1	20040504	AU 2003-282679		20031002	<--
PRIORITY APPLN. INFO.:			US 2002-416193P	P	20021004	<--
			US 2002-417120P	P	20021007	<--
			WO 2003-US31509	W	20031002	<--

OTHER SOURCE(S): MARPAT 140:357333
ED Entered STN: 23 Apr 2004
GI



I

AB Title compds. [I; R1 = alkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, benzyl, optionally substituted with ≥1 halo, OH, cyano, NO2, haloalkyl, amino, aminoalkyl, aminodialkyl, alkyl, cycloalkyl, alkoxy, phenoxy, alkenyl,

alkynyl, haloalkoxy, carboxy, carboalkoxy, alkylcarboxamido, arylcarboxamido, heteroarylcarboxamido, heterocyclic carboxamido, alkylthio, alkylsulfinyl, alkylsulfonyl, haloalkylthio, haloalkylsulfinyl, haloalklcylsulfonyl, alkylureyl, arylureyl; R2 = H, alkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, PhCH2, Ph, heteroaryl, optionally substituted with ≥1 halo, OH, cyano, nitro, haloalkyl, amino, aminoalkyl, aminodialkyl, alkyl, cycloalkyl, alkoxy, phenoxy, alkenyl, alkynyl, haloalkoxy, carboxy, carboalkoxy, alkylcarboxamido, arylcarboxamido, heteroarylcarboxamido, heterocyclic carboxamido, alkylthio, alkylsulfmyl, alkylsulfonyl, haloalkylthio, haloalkylsulfinyl, haloalkylsulfonyl, alkylureyl or arylureyl groups; Ar = (substituted) pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl], were prepared for the treatment of metabolic-related disorders, including dyslipidemia, atherosclerosis, coronary heart disease, insulin resistance, type 2 diabetes, Syndrome-X and the like (no data). Thus, nicotinyl chloride, 2-methyl-5-propyl-2,4-dihydropyrazol-3-one, and Ca(OH)2 were heated at 90° in dioxane for 2 h. to give (5-hydroxy-1-methyl-3-propyl-1H- pyrazol-4-yl)pyridin-3-ylmethanone. I may be used in combination with other active agents such α-glucosidase inhibitors, aldose reductase inhibitors, biguanides, HMG-CoA reductase inhibitors, squalene synthesis inhibitors, fibrates, LDL catabolism enhancers, angiotensin converting enzyme inhibitors, and insulin secretion enhancers.

IC ICM C07D231-00

CC 28-8 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

IT **Diabetes** mellitus
(non-insulin-dependent; preparation of aroylhydroxypyrazoles for treatment of metabolic disorders)

IT 56-03-1, Biguanide 64-77-7, Tolbutamide 94-20-2, Chloropropamide 114-86-3, Phenformin 339-43-5, Carbutamide 339-44-6, Glymidine 451-71-8, Glyhexamide 535-65-9, Glybuthiazole 631-27-6, Glyclopyramide 637-07-0, Clofibrate 657-24-9, Metformin 664-95-9, Tolcyclamide 692-13-7, Buformin 882-09-7, Clofibric acid 968-81-0, Acetohexamide 1156-19-0, Tolazamide 1228-19-9, Glypinamide 1492-02-0, Glybuzole 2295-31-0D, Thiazolidinedione, derivs 3149-00-6, Phenbutamide 4618-41-1, 1-Butyl-3-metanilylurea 10238-21-8, Glibenclamide 14929-11-4, Simfibrate 21187-98-4, Gliclazide 25046-79-1, Glisoxepid 25812-30-0, Gemfibrozil 26944-48-9, Glibornuride 29094-61-9, Glipizide 30299-08-2, Clinofibrate 31637-97-5, Etofibrate 31980-29-7, Nicofibrate 33342-05-1, Gliquidone 41859-67-0, Bezafibrate 42597-57-9, Ronifibrate, biological studies 49562-28-9, Fenofibrate 52214-84-3, Ciprofibrate 54504-70-0, Theofibrate 55285-45-5, Pirifibrate 55937-99-0, Beclobrate 56180-94-0, Acarbose 62571-86-2, Captopril 68367-52-2, Sorbinil 69047-39-8, Binifibrate 74258-86-9, Alacepril 75330-75-5, Lovastatin 75847-73-3, Enalapril 76420-72-9, Enalaprilat 76547-98-3, Lisinopril 79902-63-9, Simvastatin 81093-37-0, Pravastatin 82159-09-9, Epalrestat 82834-16-0, Perindopril 82964-04-3, Tolrestat 83435-66-9, Delapril 83480-29-9, Voglibose 83647-97-6, Spirapril 85441-61-8, Quinapril 85856-54-8, Moveltipril 86541-75-5, Benazepril 87333-19-5, Ramipril 87679-37-6, Trandolapril 88768-40-5, Cilazapril 89371-37-9, Imidapril 89391-50-4, Imirestat 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 98048-97-6, Fosinopril 105816-04-4, Nateglinide 110703-94-1, Zopolrestat 111025-46-8, Pioglitazone 111223-26-8, Ceronapril 111902-57-9, Temocapril 112733-06-9, Zenarestat 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 145375-43-5, **Mitiglinide** 145599-86-6, Cerivastatin 287714-41-4, Rosuvastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of aroylhydroxypyrazoles for treatment of metabolic disorders)

IT 9001-42-7, α-Glucosidase 9015-82-1, Angiotensin converting enzyme

9028-31-3, Aldose **reductase** 9028-35-7, HMG-CoA **reductase** 9077-14-9, Squalene synthase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (**inhibitors** coadministration; preparation of aroylhydroxypyrazoles for treatment of metabolic disorders)

L61 ANSWER 8 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:60541 HCAPLUS Full-text
DOCUMENT NUMBER: 140:105298
TITLE: Bicyclic oligopeptides and their use as glucagon receptor antagonists
INVENTOR(S): Potterat, Olivier; Streicher, Ruediger; Wagner, Klaus; Maurer, Till; Mack, Juergen; Peters, Stefan
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma GmbH & Co. KG, Germany
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004007535	A1	20040122	WO 2003-EP7657	20030715 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2489189	A1	20040122	CA 2003-2489189	20030715 <--
AU 2003246702	A1	20040202	AU 2003-246702	20030715 <--
EP 1525218	A1	20050427	EP 2003-763864	20030715 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006505507	T	20060216	JP 2004-520641	20030715 <--
US 2004072736	A1	20040415	US 2003-621272	20030717 <--
US 7101848	B2	20060905		

PRIORITY APPLN. INFO.:	EP 2002-15907	A	20020717 <--
	US 2002-416797P	P	20021008 <--
	WO 2003-EP7657	W	20030715 <--

OTHER SOURCE(S): MARPAT 140:105298
ED Entered STN: 26 Jan 2004
AB The invention relates to a bicyclic oligopeptide or ester thereof having the capability to inhibit the glucagon receptor, which essentially consists of(a) a first cyclic group, which comprises at least one cysteine group and is formed by an amide bonding of the N-terminal amino acid with the second carboxylate group of a diacid amino acid, and (b) a second cyclic group which is formed by an amide bonding of an amino acid with the -carboxylate group of said diacid amino acid, and by a disulfide bonding of the C-terminal cysteine and a cysteine group within the first cyclic group (a); and to the use of such bicyclic oligopeptides for the preparation of a medicament for the treatment or prevention of diseases, in which glucagon receptors are involved.
IC ICM C07K007-56
ICS A61K038-12; C07K014-36
CC 1-10 (Pharmacology)

Section cross-reference(s): 2, 10, 34, 63

ST bicyclic oligopeptide glucagon receptor **inhibition** disease treatment; **diabetes** treatment bicyclic oligopeptide glucagon receptor **inhibition**

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ALBP (adipocyte lipid-binding protein), **inhibitors**; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT Streptomyces
(DSM 14996, bicyclic oligopeptide from; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(SGLT2 (sodium-dependent glucose transporter 2), **inhibitors**; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT Glucagon-like peptide-1 receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonists; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT Drug delivery systems
(ampoules; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT Actinomyces
(bicyclic oligopeptide from; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT Antidiabetic agents
Antiobesity agents
Cardiovascular agents
Diabetes mellitus
Human
Peroxisome proliferators
(bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT Glucagon receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT Drug delivery systems
(capsules; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT Drug delivery systems
(carriers; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT Peptides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclic; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and

metabolic stability)

IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(modulating agents; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT Retinoid X receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(modulators; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT Drug delivery systems
(suppositories; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT Drug delivery systems
(tablets, coated; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT Drug delivery systems
(tablets; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α, modulators; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(γ, modulators; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT **145375-43-5, Mitiglinide**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(analogs; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT 9007-92-5, Glucagon, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT 647807-35-0P
RL: BSU (Biological study, unclassified); NPO (Natural product occurrence); PAC (Pharmacological activity); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT 647807-36-1P
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT 9004-10-8, Insulin, biological studies

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT 56-03-1D, Biguanide, derivs. 94-20-2, Chloropropamide 657-24-9, Metformin 10238-21-8, Glyburide 21187-98-4, Gliclazide 29094-61-9, Glipizide 56180-94-0, Acarbose 72432-03-2, Miglitol 89750-14-1, Glucagon-like peptide I 93479-97-1, Glimepiride 97322-87-7, Troglitazone 105816-04-4, Nateglinide 111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone 135062-02-1, Repaglinide 141732-76-5, Exendin-4 161600-01-7, Isaglitazone
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT 9033-06-1, Glucosidase 54249-88-6, Dipeptidyl peptidase IV 300865-11-6, Protein tyrosine phosphatase 1B 391208-93-8, Glycogen synthase kinase 3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 9 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:60532 HCAPLUS Full-text
DOCUMENT NUMBER: 140:105297
TITLE: Bicyclic oligopeptides and their use as glucagon receptor antagonists
INVENTOR(S): Potterat, Olivier; Streicher, Ruediger; Wagner, Klaus; Maurer, Till; Mack, Juergen; Peters, Stefan
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma GmbH & Co. KG, Germany
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004007524	A2	20040122	WO 2003-EP7311	20030708 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003260306	A1	20040202	AU 2003-260306	20030708 <--
US 2004072736	A1	20040415	US 2003-621272	20030717 <--
US 7101848	B2	20060905		

PRIORITY APPLN. INFO.: EP 2002-15907 A 20020717 <--
US 2002-416797P P 20021008 <--

WO 2003-EP7311 W 20030708 <--

OTHER SOURCE(S): MARPAT 140:105297
ED Entered STN: 26 Jan 2004
AB The invention relates to a bicyclic oligopeptide or ester thereof having the capability to inhibit the glucagon receptor, which essentially consists of (a) a first cyclic group, which comprises at least one cysteine group and is formed by an amide bonding of the N-terminal amino acid with the second carboxylate group of a diacid amino acid, and (b) a second cyclic group which is formed by an amide bonding of an amino acid with the -carboxylate group of said diacid amino acid, and by a disulfide bonding of the C-terminal cysteine and a cysteine group within the first cyclic group (a); and to the use of such bicyclic oligopeptides for the preparation of a medicament for the treatment or prevention of diseases, in which glucagon receptors are involved.
IC ICM C07K
CC 1-10 (Pharmacology)
Section cross-reference(s): 10, 34, 63
ST bicyclic oligopeptide glucagon receptor **inhibition** disease treatment; **diabetes** treatment bicyclic oligopeptide glucagon receptor **inhibition**
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ALBP (adipocyte lipid-binding protein), **inhibitors**; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
IT Streptomyces
(DSM 14996, bicyclic oligopeptide from; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(SGLT2 (sodium-dependent glucose transporter 2), **inhibitors**; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
IT Glucagon-like peptide-1 receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonists; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
IT Drug delivery systems
(ampoules; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
IT Actinomyces
(bicyclic oligopeptide from; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
IT Antidiabetic agents
Antiobesity agents
Cardiovascular agents
Diabetes mellitus
Human
(bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)
IT Glucagon receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and

metabolic stability)

IT Drug delivery systems
(capsules; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT Drug delivery systems
(carriers; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT Peptides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclic; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(modulating agents; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT Retinoid X receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(modulators; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT Drug delivery systems
(suppositories; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT Drug delivery systems
(tablets, coated; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT Drug delivery systems
(tablets; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α, agonists; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(γ, modulators; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT **145375-43-5, Mitiglinide**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(analogs; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT 9007-92-5, Glucagon, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT 647807-35-0P
RL: BSU (Biological study, unclassified); NPO (Natural product

occurrence); PAC (Pharmacological activity); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT 647807-36-1P
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT 56-03-1D, Biguanide, derivs. 94-20-2, Chloropropamide 657-24-9, Metformin 10238-21-8, Glyburide 21187-98-4, Gliclazide 29094-61-9, Glipizide 56180-94-0, Acarbose 72432-03-2, Miglitol 89750-14-1, Glucagon-like peptide I 93479-97-1, Glimepiride 97322-87-7, Troglitazone 105816-04-4, Nateglinide 111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone 135062-02-1, Repaglinide 141732-76-5, Exendin-4 161600-01-7, Isaglitazone
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

IT 9033-06-1, Glucosidase 54249-88-6, Dipeptidyl peptidase IV 300865-11-6, Protein tyrosine phosphatase 1B 391208-93-8, Glycogen synthase kinase 3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; bicyclic oligopeptides as glucagon receptor **inhibitors** in relation to disease treatment and combination with other agents and metabolic stability)

L61 ANSWER 10 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:20487 HCAPLUS Full-text
DOCUMENT NUMBER: 140:65256
TITLE: Drug composition for **prevention** or **inhibition** of advance of **diabetic** complication
INVENTOR(S): Mikoshiba, Imao; Suzuki, Hisao; Kiyono, Yuji
PATENT ASSIGNEE(S): Kissei Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004002474	A1	20040108	WO 2003-JP8084	20030626 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,

LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR,
TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2489660	A1	20040108	CA 2003-2489660		20030626 <--
AU 2003244083	A1	20040119	AU 2003-244083		20030626 <--
EP 1552830	A1	20050713	EP 2003-761816		20030626 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
CN 1665499	A	20050907	CN 2003-815245		20030626 <--
US 2005215607	A1	20050929	US 2004-519155		20041227 <--
PRIORITY APPLN. INFO.:			JP 2002-189559	A	20020628 <--
			WO 2003-JP8084	W	20030626 <--

ED Entered STN: 11 Jan 2004

AB Disclosed is a drug composition capable of attaining a good state of blood sugar control so as to enable correcting postprandial high blood sugar levels or high blood sugar levels at early fasting time. In particular, a drug composition for prevention or inhibition of advance of diabetic complications to be taken before meals, comprising 5 to 45 mg, in terms of one-time dose, of mitiglinide or its pharmacol. acceptable salt or a hydrate thereof, e.g., mitiglinide calcium salt hydrate. The drug composition is highly useful for the prevention or inhibition of advance of, for example, diabetic microangio complications and arteriosclerosis because the ratio of occurrence of side effects, such as low blood sugar level symptom and gastrointestinal tract disorder, is low. A tablet containing mitiglinide calcium salt hydrate 10 mg/tablet was formulated, and its effect on blood sugar level and side effect in patients with type 2 biabetes was examined

IC ICM A61K031-4035
ICS A61P003-10; A61P009-00; A61P009-10; A61P013-12; A61P027-02; A61P043-00

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

ST **mitiglinide diabetic** complication treatment oral

IT Blood vessel, disease
(**diabetic** microangiopathy; drug composition for **prevention** or **inhibition** of advance of **diabetic** complication)

IT Kidney, disease
(**diabetic** nephropathy; drug composition for **prevention** or **inhibition** of advance of **diabetic** complication)

IT Eye, disease
(**diabetic** retinopathy; drug composition for **prevention** or **inhibition** of advance of **diabetic** complication)

IT Arteriosclerosis
(**diabetic**; drug composition for **prevention** or **inhibition** of advance of **diabetic** complication)

IT Human
(drug composition for **prevention** or **inhibition** of advance of **diabetic** complication)

IT **Diabetes** mellitus
(non-insulin-dependent; drug composition for **prevention** or **inhibition** of advance of **diabetic** complication)

IT Antidiabetic agents
(oral; drug composition for **prevention** or **inhibition** of advance of **diabetic** complication)

IT Drug delivery systems
(tablets; drug composition for **prevention** or **inhibition** of advance of **diabetic** complication)

IT 50-99-7, D-Glucose, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(blood; drug composition for **prevention** or **inhibition** of advance of **diabetic** complication)
IT **145375-43-5, Mitiglinide 207844-01-7**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug composition for **prevention** or **inhibition** of advance of **diabetic** complication)
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 11 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:20486 HCAPLUS Full-text
DOCUMENT NUMBER: 140:65255
TITLE: Drug composition for blood sugar control
INVENTOR(S): Mikoshiba, Imao; Suzuki, Hisao; Kiyono, Yuji
PATENT ASSIGNEE(S): Kissei Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004002473	A1	20040108	WO 2003-JP8083	20030626
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2490250	A1	20040108	CA 2003-2490250	20030626
AU 2003244082	A1	20040119	AU 2003-244082	20030626
EP 1532979	A1	20050525	EP 2003-761815	20030626
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1665498	A	20050907	CN 2003-815244	20030626
US 2005267195	A1	20051201	US 2004-519102	20041227
PRIORITY APPLN. INFO.:			JP 2002-189556 A	20020628
			WO 2003-JP8083 W	20030626

ED Entered STN: 11 Jan 2004
AB Disclosed is a drug composition capable of attaining a good state of blood sugar control so as to enable correcting postprandial high blood sugar levels or high blood sugar levels at early fasting time. In particular, a drug composition for blood sugar control to be taken before meals, comprising 5 to 45 mg, in terms of one-time dose, of mitiglinide or its pharmacol. acceptable salt or a hydrate thereof, e.g., mitiglinide calcium salt hydrate. The drug composition is highly useful for the prevention and treatment of, for example, type 2 diabetes because the ratio of occurrence of side effects, such as low blood sugar level symptom and gastrointestinal tract disorder, is low. A tablet containing mitiglinide calcium salt hydrate 10 mg/tablet was formulated, and its effect on blood sugar level and side effect in patients with type 2 diabetes was examined

IC ICM A61K031-4035
ICS A61P003-10; A61P043-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
ST **mitiglinide** oral type 2 antidiabetic
IT Human
Hyperglycemia
(drug composition for blood sugar control containing **mitiglinide**)
IT Diabetes mellitus
(non-insulin-dependent; drug composition for blood sugar control containing **mitiglinide**)
IT Antidiabetic agents
(oral; drug composition for blood sugar control containing **mitiglinide**)
IT Drug delivery systems
(tablets; drug composition for blood sugar control containing **mitiglinide**)
IT 50-99-7, D-Glucose, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(blood; drug composition for blood sugar control containing **mitiglinide**)
IT **145375-43-5, Mitiglinide 207844-01-7**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug composition for blood sugar control containing **mitiglinide**)
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 12 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:496322 HCAPLUS Full-text
DOCUMENT NUMBER: 141:167555
TITLE: Rapid-onset hypoglycemic effect of **mitiglinide** calcium dihydrate (KAD-1229), a novel antipostprandial-**hyperglycemia** agent. comparison with glimepiride
AUTHOR(S): Ojima, Kazuma; Aoyagi, Ikumi; Fujimori, Yoshikazu; Ichikawa, Kiyoshi; Kusama, Hiroshi; Kojima, Masami; Nagasawa, Tatsuya; Ohta, Masanao; Okuhara, Yuji; Kobayashi, Maiko; Tamura, Kei; Kuroda, Junji; Shibata, Nobuo
CORPORATE SOURCE: Pharmacology Research Lab. R&D, Kissei Pharmaceutical Co., Ltd., Japan
SOURCE: Japanese Pharmacology & Therapeutics (2004), 32(3), 161-167
CODEN: JPTABU
PUBLISHER: Raifu Saiensu Shuppan K.K.
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
ED Entered STN: 21 Jun 2004
AB The purpose of the present study was to evaluate the hypoglycemic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostprandial-hyperglycemia agent, by comparing it with that of glimepiride, a sulfonylurea agent. In fasted beagle dogs, KAD-1229 (0.15, 0.3 mg/kg) or glimepiride (0.03, 0.06 mg/kg) was administered orally either with no load or just before an oral glucose load. Blood samples were taken from the cephalic vein for the determination of plasma glucose levels. In expts. with no load, plasma insulin levels were also measured. With no glucose load, the hypoglycemic effect of KAD-1229 had a faster onset (at 0.25 h) than that of glimepiride (at 1 h), and a shorter duration (0.25-1 h) than that of glimepiride (1-8 h). KAD-1229 stimulated insulin secretion, the peak level occurring within 0.25 h

and a return to baseline within 1 h. In contrast, the peak insulin level occurred at 1 h post-dose in the glimepiride groups. In the oral glucose tolerance test, KAD-1229 rapidly inhibited the increase in plasma glucose (at 0.25 h), and its effect had disappeared within 2 h after its administration. Glimepiride induced a lowering of the plasma glucose level at 1 h after its administration, and at a dose of 0.06 mg/kg, the glucose level given did not return to control values within 8 h. The hypoglycemic effect of KAD-1229 was clearly faster in onset and shorter lasting than that of glimepiride. KAD-1229 can be expected to be more effective than glimepiride at normalizing postprandial hyperglycemia.

CC 1-10 (Pharmacology)

IT Antidiabetic agents
Diabetes mellitus
(rapid-onset hypoglycemic effect of **mitiglinide** calcium dihydrate (KAD-1229), a novel antipostprandial-**hyperglycemia** agent. comparison with glimepiride)

IT 50-99-7, D-Glucose, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(blood; rapid-onset hypoglycemic effect of **mitiglinide** calcium dihydrate (KAD-1229), a novel antipostprandial-**hyperglycemia** agent. comparison with glimepiride)

IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(rapid-onset hypoglycemic effect of **mitiglinide** calcium dihydrate (KAD-1229), a novel antipostprandial-**hyperglycemia** agent. comparison with glimepiride)

IT 93479-97-1, Glimepiride 145525-41-3, KAD-1229
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rapid-onset hypoglycemic effect of **mitiglinide** calcium dihydrate (KAD-1229), a novel antipostprandial-**hyperglycemia** agent. comparison with glimepiride)

L61 ANSWER 13 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:345396 HCAPLUS Full-text
DOCUMENT NUMBER: 141:325483
TITLE: Rapid onset-insulinotropic effect of **mitiglinide** calcium dihydrate (KAD-1229), a novel antipostpradial **hyperglycemic** agent: comparison with nateglinide
AUTHOR(S): Ojima, Kazuma; Ichikawa, Kiyoshi; Fujimori, Yoshikazu; Aoyagi, Ikumi; Yamato, Tokuhisa; Tsuji, Atsutoshi; Kusama, Hiroshi; Kojima, Masami; Shibata, Nobuo
CORPORATE SOURCE: Pharmacology Research R & D, Kissei Pharmaceutical Co., Ltd., Japan
SOURCE: Japanese Pharmacology & Therapeutics (2004), 32(2), 73-80
CODEN: JPTABU
PUBLISHER: Raifu Saiensu Shuppan K.K.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 28 Apr 2004
AB Objectives: The purpose of the present study was to evaluate the insulinotropic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostprandial hyperglycemic agent, by comparison with that of nateglinide. Methods: Mitiglinide calcium dihydrate or nateglinide was administered orally just before an oral-sucrose or liquid-meal load in normal rats, and in mild, moderate, or severe streptozotocin-injected diabetic rats. The plasma insulin and glucose levels were measured. Results: Mitiglinide calcium dihydrate (1 mg/kg) and nateglinide (50 mg/kg) decreased the plasma glucose levels

significantly at 15-120 min and 15-60 min, resp. in normal rats, and at 30-90 min and 30-60 min, resp., in mildly diabetic rats. These drugs increased the plasma insulin levels at 5-45 min and 5-15 min, resp., in normal rats, and at 15-60 min and 15-45 min, resp., in mildly diabetic rats. In moderately diabetic rats, the antihyperglycemic effects of mitiglinide calcium dihydrate (1 and 3 mg/kg) and nateglinide (50 and 100 mg/kg) were evident at 30-120 min and 30-60 min, resp. In the same rats, mitiglinide, but not nateglinide, significantly increased the plasma insulin levels at 30 min after its administration. Mitiglinide also exhibited antihyperglycemic and insulinotropic effects in the severely diabetic rats. Conclusion: Mitiglinide and nateglinide are suitable drugs for controlling postprandial hyperglycemia. Their antihyperglycemic effects were probably secondary to their rapid-onset, short-lasting insulinotropic effects, and mitiglinide seemed to be a more potent rapid-onset insulinotropic drug than nateglinide.

CC 1-10 (Pharmacology)

ST insulinotropic **mitiglinide** calcium dihydrate KAD1229
antipostpradial **hyperglycemia** nateglinide

IT Antidiabetic agents
Hyperglycemia
(rapid onset-insulinotropic effect of **mitiglinide** calcium dihydrate (KAD-1229), a novel antipostpradial **hyperglycemic** agent: comparison with nateglinide)

IT 105816-04-4, Nateglinide 145525-41-3, KAD-1229
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rapid onset-insulinotropic effect of **mitiglinide** calcium dihydrate (KAD-1229), a novel antipostpradial **hyperglycemic** agent: comparison with nateglinide)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 14 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:931184 HCAPLUS Full-text
DOCUMENT NUMBER: 140:8791
TITLE: Therapeutic agent for **diabetes**
INVENTOR(S): Nakanishi, Satoshi; Yano, Hiroshi; Mori, Kiyotoshi; Ogino, Fumiko; Kusaka, Hideaki; Ueno, Kimihisa; Nomoto, Yuji; Matsuda, Yuzuru
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003097064	A1	20031127	WO 2003-JP6136	20030516 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003234929	A1	20031202	AU 2003-234929	20030516 <--

PRIORITY APPLN. INFO.: JP 2002-143598 A 20020517 <--
WO 2003-JP6136 W 20030516 <--

OTHER SOURCE(S): MARPAT 140:8791
ED Entered STN: 28 Nov 2003
AB A therapeutic agent for diabetes, is characterized by containing at least one member selected among sulfonylurea antidiabetic agents and sulfonylurea-free K+ ATP channel blocker antidiabetic agents and at least one member selected among a fused purine derivative and pharmacol. acceptable salts of these. For example, a tablet contained glibenclamide 2, (R)-2-cyclopentyl-7,8-dihydro-8-(4-picolyl)-4-propyl-1H-imidazo[2,1-i]- purin-5(4H)-one d-tartaric acid salt 18, lactose 143.4, starch 30, hydroxypropyl cellulose 6, and Mg stearate 0.6 mg.
IC ICM A61K031-522
ICS A61K031-198; A61K031-4453; A61K031-64; A61K045-00; A61P003-10
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
ST antidiabetic sulfonylurea potassium channel **blocker** purine deriv; tablet glibenclamide imidazopurine deriv antidiabetic combination
IT Potassium channel **blockers**
(ATP-sensitive; antidiabetic combinations for treatment and **prevention** of **diabetes** complications and side effects)
IT Sulfonylureas
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antidiabetic combinations for treatment and **prevention** of **diabetes** complications and side effects)
IT Drug delivery systems
(capsules; antidiabetic combinations for treatment and **prevention** of **diabetes** complications and side effects)
IT Drug delivery systems
(tablets; antidiabetic combinations for treatment and **prevention** of **diabetes** complications and side effects)
IT 64-77-7, Tolbutamide 94-20-2, Chlorpropamide 339-43-5, Carbutamide 631-27-6, Glyclopyramide 664-95-9, Glycyclamide 968-81-0, Acetohexamide 1156-19-0, Tolazamide 1492-02-0, Glybuzol 10238-21-8, Glibenclamide 21187-98-4, Gliclazide 24477-37-0, Glisolamide 25046-79-1, Glisoxepide 26944-48-9, Glibornuride 29094-61-9, Glipizide 32797-92-5, Glisentide 33342-05-1, Gliquidone 93479-97-1, Glimepiride 105816-04-4, Nateglinide 135062-02-1, Repaglinide 145375-43-5, **Mitiglinide** 254426-47-6 348165-49-1 348362-73-2 349554-62-7 349554-69-4 627512-37-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antidiabetic combinations for treatment and **prevention** of **diabetes** complications and side effects)
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 15 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:777602 HCAPLUS Full-text
DOCUMENT NUMBER: 139:296975
TITLE: Combination of a HMG-CoA **reductase** **inhibitor** and an insulin secretion enhancer
INVENTOR(S): Damon, Robert Edson; Hughes, Thomas Edward; Burkey, Bryan
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SOURCE: PCT Int. Appl., 32 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003080070	A2	20031002	WO 2003-EP2978	20030321 <--
WO 2003080070	A3	20040325		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
CA 2479880	A1	20031002	CA 2003-2479880	20030321 <--
AU 2003209745	A1	20031008	AU 2003-209745	20030321 <--
US 2004002519	A1	20040101	US 2003-393798	20030321 <--
EP 1523316	A2	20050420	EP 2003-744834	20030321 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1642559	A	20050720	CN 2003-806655	20030321 <--
JP 2005526788	T	20050908	JP 2003-577896	20030321 <--
BR 2003008613	A	20050301	BR 2003-8613	20030324 <--
NO 2004004487	A	20041220	NO 2004-4487	20041020 <--
US 2007027197	A1	20070201	US 2006-497130	20060801 <--
PRIORITY APPLN. INFO.:			US 2002-366752P P	20020322 <--
			US 2003-393798 B1	20030321 <--
			WO 2003-EP2978 W	20030321 <--

ED Entered STN: 03 Oct 2003

AB The present invention relates to a combination pharmaceutical composition comprising as active ingredients (i) a HMG-CoA reductase inhibitor or a salt, (ii) (a) an insulin secretion enhancer or a salt or (b) an insulin sensitizer or a salt. Thus, capsules contained fluvastatin sodium 42.962, CaCO3 125.680, NaHCO3 4.000, microcryst. cellulose 114.440, pregelatinized starch 83.800, Mg stearate 21.00, and talc 18.860 mg, and water qs.

IC ICM A61K031-64
ICS A61K031-40; A61K031-015; A61K031-435; A61K031-21; A61P005-50; A61K031-404; A61K031-155; A61P003-00

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

ST insulin secretion enhancer HMGCoA **reductase inhibitor**

IT Drug delivery systems
(capsules; combination of HMG-CoA **reductase inhibitor** and insulin secretion enhancer)

IT Antiarteriosclerotics
Antidiabetic agents
Antihypertensives
Antiobesity agents
Atherosclerosis
Hypertension
Hypolipemic agents
Hypothyroidism
Kidney, disease
Obesity
(combination of HMG-CoA **reductase inhibitor** and insulin secretion enhancer)

IT Dyslipidemia
Hyperlipidemia
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(combination of HMG-CoA **reductase inhibitor** and insulin secretion enhancer)

IT Sulfonylureas
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of HMG-CoA **reductase inhibitor** and insulin secretion enhancer)

IT Artery, disease
(coronary; combination of HMG-CoA **reductase inhibitor** and insulin secretion enhancer)

IT Kidney, disease
(failure; combination of HMG-CoA **reductase inhibitor** and insulin secretion enhancer)

IT Liver, disease
(fatty; combination of HMG-CoA **reductase inhibitor** and insulin secretion enhancer)

IT Heart, disease
(infarction, survival post; combination of HMG-CoA **reductase inhibitor** and insulin secretion enhancer)

IT Metabolic disorders
(metabolic syndrome X; combination of HMG-CoA **reductase inhibitor** and insulin secretion enhancer)

IT **Diabetes** mellitus
(non-insulin-dependent; combination of HMG-CoA **reductase inhibitor** and insulin secretion enhancer)

IT Ovary, disease
(polycystic; combination of HMG-CoA **reductase inhibitor** and insulin secretion enhancer)

IT Drug delivery systems
(tablets; combination of HMG-CoA **reductase inhibitor** and insulin secretion enhancer)

IT 64-77-7, Tolbutamide 94-20-2, Chlorpropamide 339-43-5, Carbutamide 451-71-8, Glyhexamide 535-65-9, Glybuthiazole 631-27-6 657-24-9, Metformin 664-95-9, Tolcyclamide 968-81-0, Acetohexamide 1156-19-0, Tolazamide 1228-19-9, Glypinamide 1492-02-0, Glybuzole 3149-00-6, Phenbutamide 3459-20-9, Glymidine 4618-41-1, 1-Butyl-3-metanilylurea 10238-21-8, Glibenclamide 21187-98-4, Gliclazide 25046-79-1, Glisoxepid 26944-48-9, Glibornuride 29094-61-9, Glipizide 33342-05-1, Gliquidone 75330-75-5, Lovastatin 79902-63-9, Simvastatin 81093-37-0, Pravastatin 89750-14-1, GLP-1 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 93957-55-2, Fluvastatin sodium 105816-04-4, Starlix DS 123475-27-4 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 138347-77-0 **145375-43-5, Mitiglinide** 145599-86-6, Cerivastatin 147511-69-1, Pitavastatin 207556-62-5 223607-24-7 274901-16-5 287714-41-4, Rosuvastatin 352513-61-2 355393-49-6 355393-50-9 355393-52-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of HMG-CoA **reductase inhibitor** and insulin secretion enhancer)

IT 9028-35-7, HMG-CoA **reductase** 54249-88-6, DPP-IV
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitor**; combination of HMG-CoA **reductase inhibitor** and insulin secretion enhancer)

IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(secretion enhancer; combination of HMG-CoA **reductase inhibitor** and insulin secretion enhancer)

L61 ANSWER 16 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:511859 HCAPLUS Full-text
DOCUMENT NUMBER: 139:90459
TITLE: Use of an immediate-release powder in pharmaceutical and nutraceutical compositions
INVENTOR(S): Besse, Jerome; Besse, Laurence
PATENT ASSIGNEE(S): Fr.
SOURCE: U.S. Pat. Appl. Publ., 5 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003124191	A1	20030703	US 2002-106923	20020325 <--
FR 2834212	A1	20030704	FR 2001-16934	20011227 <--
FR 2834212	B1	20040709		
CA 2471903	A1	20030710	CA 2002-2471903	20021227 <--
WO 2003055464	A1	20030710	WO 2002-FR4575	20021227 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002364489	A1	20030715	AU 2002-364489	20021227 <--
EP 1458356	A1	20040922	EP 2002-799854	20021227 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002015380	A	20041207	BR 2002-15380	20021227 <--
US 2005118272	A1	20050602	US 2003-500213	20021227 <--
JP 2005520799	T	20050714	JP 2003-556042	20021227 <--
HU 200500509	A2	20050928	HU 2005-509	20021227 <--
NO 2004003172	A	20040914	NO 2004-3172	20040726 <--
PRIORITY APPLN. INFO.:			FR 2001-16934 A	20011227 <--
			WO 2002-FR4575 W	20021227 <--

ED Entered STN: 04 Jul 2003
AB The present invention relates to the use of a powder comprising at least one active substance, at least one surfactant, at least one wetting agent and at least one diluent, for preparing a pharmaceutical or nutraceutical composition, this composition allowing rapid and immediate release of the active substance. Granules containing phloroglucinol 10, sorbitol 89, and propylene glycol 1% were prepared
IC ICM A61K031-7048
ICS A61K031-56; A61K031-522; A61K031-4965; A61K031-445; A61K031-573; A61K031-496; A61K031-4178; A61K031-135
INCL 424489000; 514182000; 514177000; 514178000; 514029000; 514649000; 514317000; 514343000; 514263350; 514554000
CC 63-6 (Pharmaceuticals)
IT **Diabetes** mellitus
(non-insulin-dependent; use of immediate-release powder in pharmaceutical and nutraceutical compns.)
IT 39391-18-9, Cyclooxygenase
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**inhibitors**; use of immediate-release powder in pharmaceutical and nutraceutical compns.)

IT 50-03-3, Hydrocortisone acetate 50-23-7, Hydrocortisone 50-28-2, Oestradiol, biological studies 50-28-2D, Oestradiol, derivs. 50-70-4, Sorbitol, biological studies 50-99-7, Dextrose, biological studies 51-34-3, Scopolamine 51-98-9, Norethisterone acetate 54-11-5, Nicotine 54-21-7, Sodium salicylate 55-63-0, Trinitrin 56-81-5, Glycerol, biological studies 57-09-0, Cetrimonium bromide 57-13-6, Urea, biological studies 57-47-6, Physostigmine 57-48-7, Fructose, biological studies 57-50-1, Sucrose, biological studies 57-55-6, Propylene glycol, biological studies 57-63-6, Ethinyl oestradiol 57-83-0, Progesterone, biological studies 58-08-2, Caffeine, biological studies 58-22-0, Testosterone 59-66-5, Acetazolamide 60-40-2, Mecamylamine 63-42-3, Lactose 64-17-5, Ethanol, biological studies 67-73-2, Fluocinolone acetonide 69-65-8, Mannitol 71-52-3, Bicarbonate, biological studies 81-13-0, Dexpanthenol 87-33-2, Isosorbide dinitrate 87-99-0, Xylitol 89-78-1, Menthol) 94-36-0, Benzoyl peroxide, biological studies 97-53-0, Eugenol 101-20-2, Triclocarban 106-24-1, Geraniol 106-25-2, Nerol 106-60-5, 5-Aminolevulinic acid 108-73-6, Phloroglucinol 110-27-0, Isopropyl myristate 112-62-9, Methyl oleate 112-80-1, Oleic acid, biological studies 113-45-1, Methyl phenidate 114-07-8, Erythromycin 123-03-5, Cetylpyridinium chloride 124-94-7, Triamcinolone 137-58-6, Lidocaine 139-33-3 143-07-7, Lauric acid, biological studies 144-80-9, Sulphacetamide 145-42-6, Sodium taurocholate 147-24-0, Diphenhydramine hydrochloride 151-21-3, Sodium lauryl sulphate, biological studies 152-97-6, Fluocortolone 302-79-4, Tretinoin 303-40-2, Fluocortolone hexanoate 356-12-7, Fluocinolide 437-38-7, Fentanyl 443-48-1, Metronidazole 470-82-6, Eucalyptol 471-34-1, Calcium carbonate, biological studies 497-19-8, Sodium carbonate, biological studies 521-18-6, Dihydrotestosterone 585-86-4, Lactitol 611-53-0, Ibacitabine 638-94-8, Desonide 645-92-1 745-65-3, Alprostadil 797-63-7, Levonorgestrel 863-57-0, Sodium glycocholate 1180-95-6, Sodium taurodeoxycholate 2002-29-1, Flumetasone pivalate 2152-44-5, Betamethasone valerate 2438-72-4, Bufexamac 3764-87-2 4205-90-7, Clonidine 4394-00-7, Nifluminic acid 4759-48-2, Isotretinoin 4985-25-5, Pyrazinobutazone 5104-49-4, Flurbiprofen 5593-20-4, Betamethasone dipropionate 5633-20-5, Oxybutynin 5716-20-1, Bamethan sulfate 6805-41-0, Escin 7757-93-9, Dibasic calcium phosphate 7758-87-4, Tribasic calcium phosphate 7759-35-5, Nestorone 7778-18-9, Calcium sulphate 9000-30-0, Guar gum 9002-72-6, Growth hormone 9003-39-8, Povidone 9004-10-8, Insulin, biological studies 9004-32-4, Sodium carboxymethylcellulose 9004-53-9, Dextrins 9004-57-3, Ethylcellulose 9004-65-3, Hydroxypropylmethylcellulose 9004-67-5, Methylcellulose 9005-25-8, Starch, biological studies 9005-32-7, Alginic acid 9005-63-4D, Polyoxyethylene sorbitan, esters with fatty acids 9005-65-6, Polysorbate 80 9042-14-2, Dextran sulphate 9087-70-1, Aprotinin 12619-70-4, Cyclodextrins 12794-10-4, Benzodiazepine 14611-51-9, Selegiline 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 16409-34-0, Sodium glycodeoxycholate 18559-94-9, Salbutamol 19216-56-9, Prazosin 22071-15-4, Ketoprofen 22832-87-7, Miconazole nitrate 22916-47-8, Miconazole 23674-86-4, Difluprednate 24169-02-6, Econazole nitrate 25122-46-7, Clobetasol propionate 25322-68-3, Polyethylene glycol 25655-41-8, Povidone Iodine 25717-80-0, Molsidomine 28981-97-7, Alprozolam 29205-06-9, Fluocortolone pivalate 29679-58-1, Fenoprofen 29984-33-6, Vidarabine monophosphate 34580-13-7, Ketotifen 36322-90-4, Piroxicam 36505-84-7, Buspirone 38304-91-5, Minoxidil 39219-28-8, Promestriene 39404-33-6, Dextrates 39809-25-1, Penciclovir 41570-61-0, Tulobuterol 51022-69-6, Amcinonide 52485-79-7, Buprenorphine 53016-31-2,

Norelgestromin 59198-70-8, Diflucortolone Valerate 59227-89-3, Azone 59277-89-3, Acyclovir 60282-87-3, Gestodene 65277-42-1, Ketoconazole 66104-22-1, Pergolide 66734-13-2, Alclometasone dipropionate 72522-13-5, Eptazocine 74103-06-3, Ketorolac 80214-83-1, Roxithromycin 99011-02-6, Imiquimod 99755-59-6, Rotigotine 106685-40-9, Adapalene 113775-47-6, Dexmedetomidine 118292-40-3, Tazarotene 119141-88-7, Esomeprazole 122852-42-0, Alosetron 129722-12-9, Aripiprazole 133099-04-4, Darifenacin 137234-62-9, Voriconazole 141563-69-1, OrZel 143322-58-1, Eletriptan 145158-71-0, Tegaserod 145209-50-3, Thiatolserine **145375-43-5**, **Mitiglinide** 147511-69-1, Pitavastatin 147657-22-5, Calcipotriol monohydrate 153259-65-5, Cilomilast 154189-24-9, Viozan 159776-70-2, Melagatran 163222-33-1 167305-00-2, Omapatrilat 178979-85-6, Capravirine 179463-17-3, Caspofungin acetate 181695-72-7, Valdecoxib 198470-84-7, Parecoxib 202409-33-4, Etoricoxib 287714-41-4, Rosuvastatin 552881-25-1, Crilanomer
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of immediate-release powder in pharmaceutical and nutraceutical compns.)

L61 ANSWER 17 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:473243 HCAPLUS Full-text
DOCUMENT NUMBER: 139:41849
TITLE: Pharmaceutical compositions containing a renin **inhibitor** and antidiabetics
INVENTOR(S): Webb, Randy Lee
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 7 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
US 2003114389	A1	20030619	US 2002-290651		20021108	<--
US 2005101638	A1	20050512	US 2004-14141		20041216	<--
US 2007093431	A1	20070426	US 2006-614401		20061221	<--
PRIORITY APPLN. INFO.:			US 2001-350708P	P	20011113	<--
			US 2002-290651	B1	20021108	<--
			US 2004-14141	A1	20041216	

ED Entered STN: 20 Jun 2003
AB The invention relates to a composition comprising a renin inhibitor (e.g., aliskiren) or a salt thereof and at least 1 antidiabetic agent. Thus, a hemifumarate of aliskiren 1000, corn starch 680, colloidal silica 200, Mg stearate 20, stearic acid 50, sodium carboxymethyl starch 250, and water qs to 1000 g.
IC ICM A61K038-04
ICS A61K031-4439; A61K031-426; A61K031-175; A61K031-16
INCL 514019000; 514342000; 514369000; 514592000; 514629000
CC 63-6 (Pharmaceuticals)
ST pharmaceutical antidiabetic renin **inhibitor**; aliskiren renin **inhibitor** pharmaceutical
IT Antidiabetic agents
Diabetes mellitus
Drug delivery systems
(pharmaceutical compns. containing renin **inhibitor** and antidiabetics)
IT Sulfonylureas

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. containing renin **inhibitor** and antidiabetics)

IT Drug delivery systems
(tablets, coated; pharmaceutical compns. containing renin **inhibitor** and antidiabetics)

IT Drug delivery systems
(tablets; pharmaceutical compns. containing renin **inhibitor** and antidiabetics)

IT 9015-94-5, Renin, biological studies 54249-88-6, DPP-IV
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitor**; pharmaceutical compns. containing renin **inhibitor** and antidiabetics)

IT 89750-14-1, GLP1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pharmaceutical compns. containing renin **inhibitor** and antidiabetics)

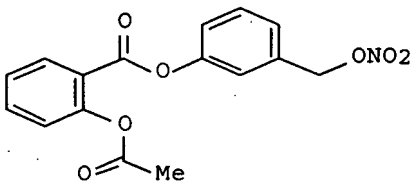
IT 657-24-9, Metformin 105816-04-4, Nateglinide 111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone 135062-02-1, Repaglinide **145375-43-5**, **Mitiglinide** 173334-57-1, Aliskiren 173334-58-2
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. containing renin **inhibitor** and antidiabetics)

IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(secretion enhancer; pharmaceutical compns. containing renin **inhibitor** and antidiabetics)

L61 ANSWER 18 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:293592 HCAPLUS Full-text
DOCUMENT NUMBER: 136:325420
TITLE: Drugs for **diabetes**, especially type 2, comprising an antiinflammatory or analgesic drug, selected bivalent linkers, and a nitrate ester
INVENTOR(S): Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030867	A2	20020418	WO 2001-EP11665	20011009 <--
WO 2002030867	A3	20020725		
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IT 2000MI2201	A1	20020412	IT 2000-MI2201	20001012 <--
IT 1319201	B1	20030926		
CA 2425655	A1	20020418	CA 2001-2425655	20011009 <--
AU 200214006	A	20020422	AU 2002-14006	20011009 <--
EP 1324974	A2	20030709	EP 2001-982414	20011009 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2004511456 T 20040415 JP 2002-534256 20011009 <--
US 2004023890 A1 20040205 US 2003-398511 20030411 <--
PRIORITY APPLN. INFO.: IT 2000-MI2201 A 20001012 <--
WO 2001-EP11665 W 20011009 <--
OTHER SOURCE(S): MARPAT 136:325420
ED Entered STN: 19 Apr 2002
GI



II

AB Useful for the treatment of diabetes, particularly type 2, are compds. or salts thereof, having the following general formula A-(B)n-(C)m-NO2 [I; wherein A = radical of a drug having an antiinflammatory or analgesic activity; B = bivalent linking group wherein the precursor must meet certain tests described in the application; C = another defined bivalent linking group; n and m = 0 or 1, provided that (n + m) = 1 or 2]. I can be used in conjunction with other antidiabetic drugs, particularly insulin. I increase the direct antidiabetic effect of insulin, and reduce complications of diabetes, particularly vascular diseases, retinopathies, neuropathies, etc.. The values of n and m, i.e., the presence or absence of bivalent linkers B and C, alone or in combination, are based on performance of the precursors of the linkers in certain tests (no data). These tests are designated as follows: (test 4A): inhibition by > 15% of hemolysis of rat erythrocytes induced by cumene hydroperoxide; (test 5): inhibition of radical production by ≥ 50% in the oxidative degradation of . desoxyribose in aqueous Fe2+(NH4)2(SO4)2/thiobarbituric acid solution; and (test 4): inhibition by ≥ 50% of DPPH-induced radical production in MeOH solution For instance, acetylsalicylic acid chloride was esterified with 3-(hydroxymethyl)phenol (80%), followed by nitation of the resultant Ph ester with HNO3/H2SO4 (82%), to give invention compound II, which is thus the 3-(nitrooxymethyl)phenyl ester of aspirin. When tested on isolated aorta from insulin-resistant rats, compound II at a concentration of 10-4 M gave 70% vasorelaxation, relative to non-insulin-resistant controls. This effect was unchanged by the presence or absence of the irreversible NO synthetase inhibitor LNNA. In contrast, both Na nitroprussiate and the indomethacin analog of II, known NO donors, were inactive, and the antidiabetic drug metformin was inactivated by LNNA.

IC ICM C07C203-04
ICS A61K031-04; A61K031-621; A61P003-10
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

IT **Diabetes** mellitus
(non-insulin-dependent, treatment; preparation of antidiabetic agents comprising antiinflammatory or analgesic drugs, selected bivalent linkers, and nitrate esters)

IT 50-81-7, Ascorbic acid, properties 52-67-5, Penicillamine 52-90-4, Cysteine, properties 56-69-9, 5-Hydroxytryptophan 56-84-8, Aspartic acid, properties 57-50-1, Saccharose, properties 60-00-4, Edetic acid, properties 60-24-2, 2-Mercaptoethanol 70-18-8, Glutathione, properties

71-00-1, Histidine, properties 77-92-9, Citric acid, properties 80-72-8, **Reductic** acid 89-65-6, Isoascorbic acid 105-59-9, N-Methyldiethanolamine 110-15-6, Succinic acid, properties 110-17-8, Fumaric acid, properties 110-63-4, 1,4-Butanediol, properties 111-17-1, 3,3'-Thiodipropionic acid 111-46-6, Diethylene glycol, properties 111-48-8, Thiodiethylene glycol 117-39-5, Quercetin 120-05-8, Sulfuretin 121-34-6, Vanillic acid 121-79-9, Propyl gallate 123-31-9, Hydroquinone, properties 141-90-2, 2-Thiouracil 149-91-7, Gallic acid, properties 154-23-4, Catechin 303-45-7, Gossypol 305-84-0, L-Carnosine 331-39-5, Caffeic acid 444-27-9, 4-Thiazolidinecarboxylic acid 458-35-5, Coniferyl alcohol 490-79-9, Gentisic acid 500-38-9, Nordihydroguaiaretic acid 501-94-0 520-18-3, Kaempferol 520-26-3, Hesperidin 526-84-1, Dihydroxymaleic acid 533-73-3, Hydroxyhydroquinone 584-85-0, Anserine 591-81-1, 4-Hydroxybutyric acid 635-65-4, Bilirubin, properties 824-46-4, Methoxyhydroquinone 1005-72-7, Tetrahydropyran-2,6-dimethanol 1077-28-7, Thioctic acid 1191-25-9, 6-Hydroxyhexanoic acid 1406-18-4, Vitamin E 1464-42-2, Selenomethionine 3614-08-2, Selenocysteine 3690-05-9, p-Cumaric alcohol 6007-86-9, Thiophene-2,5-dimethanol 7400-08-0, p-Cumaric acid 15537-71-0, N-Acetylpenicillamine 19750-45-9, 2-Oxo-4-thiazolidinecarboxylic acid 54120-69-3, 1,4-Dioxan-2,6-dimethanol 54573-75-0, 1α-OH-Vitamin D2 55721-11-4, Secalciferol 63147-28-4, 3,5-Di-tert-butyl-4-hydroxybenzyl thioglycolate 83805-11-2, Flocalcitriol 92614-59-0, Glutathione ethyl ester 97451-46-2, Glutathione isopropyl ester 103909-75-7, 22-Oxacalcitriol 148258-92-8 326850-58-2, Tetrahydrothiopyran-2,6-dimethanol 326850-59-3, 1,4-Dithiane-2,6-dimethanol 326850-60-6, Cyclohexene-1,5-dimethanol 326850-61-7, Thiazole-2,5-dimethanol 326850-62-8, Oxazole-2,5-dimethanol 414355-30-9, 4H-Pyran-2,6-dimethanol
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bivalent linker precursor; preparation of antidiabetic agents comprising antiinflammatory or analgesic drugs, selected bivalent linkers, and nitrate esters)

IT 50-78-2DP, Acetylsalicylic acid, nitroxyl-containing derivs. 61-68-7DP, Mefenamic acid, nitroxyl-containing derivs. 65-45-2DP, Salicylamide, nitroxyl-containing derivs. 69-72-7DP, Salicylic acid, nitroxyl-containing derivs. 89-45-2DP, Salicylsulfuric acid, nitroxyl-containing derivs. 118-55-8DP, Phenyl salicylate, nitroxyl-containing derivs. 118-57-0DP, Acetaminosalol, nitroxyl-containing derivs. 487-48-9DP, Salacetamide, nitroxyl-containing derivs. 530-75-6DP, Acetylsalicylsalicylic acid, nitroxyl-containing derivs. 530-78-9DP, Flufenamic acid, nitroxyl-containing derivs. 552-94-3DP, Salsalate, nitroxyl-containing derivs. 644-62-2DP, Meclofenamic acid, nitroxyl-containing derivs. 695-34-1DP, 2-Amino-4-picoline, nitroxyl-containing derivs. 1503-53-3DP, 5-Bromosalicylic acid acetate, nitroxyl-containing derivs. 4394-00-7DP, Niflumic acid, nitroxyl-containing derivs. 5104-49-4DP, Flurbiprofen, nitroxyl-containing derivs. 13710-19-5DP, Tolfenamic acid, nitroxyl-containing derivs. 15687-27-1DP, Ibuprofen, nitroxyl-containing derivs. 38194-50-2DP, Sulindac, nitroxyl-containing derivs. 38677-85-9DP, Flunixin, nitroxyl-containing derivs. 87893-55-8DP, 15-Deoxy-Δ12,14-prostaglandin, nitroxyl-containing derivs. 105816-04-4DP, Nateglinide, nitroxyl-containing derivs. 135062-02-1DP, Repaglinide, nitroxyl-containing derivs. **145375-43-5DP, Mitiglinide**, nitroxyl-containing derivs. 177785-17-0DP, (S)-4-[2-(2-Benzoxazolylmethylamino)ethoxy]-α-(2,2,2-trifluoroethoxy)benzenepropanoic acid, nitroxyl-containing derivs. 195137-72-5DP, JTT-608, nitroxyl-containing derivs. 196808-24-9DP, N-(2-Benzoylphenyl)-O-[2-(methyl-2-pyridinylamino)ethyl]-L-tyrosine,

nitroxyl-containing derivs. 196808-45-4DP, Farglitazar, nitroxyl-containing derivs. 236111-01-6DP, (S)-4-[2-(2-Benzoxazolylmethylamino)ethoxy]-α-ethoxybenzenepropanoic acid, nitroxyl-containing derivs. 267412-60-2DP, (2S,5S)-N,N-Dibenzyl-3-[4-(4-Carboxyphenyl)butyl]-2-heptyl-4-oxothiazolidine-5-acetamide, nitroxyl-containing derivs. 403731-62-4DP, Rosiglitazone nitrate, nitroxyl-containing derivs. 414355-31-0DP, Pioglitazone nitrate, nitroxyl-containing derivs.
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidates; preparation of antidiabetic agents comprising antiinflammatory or analgesic drugs, selected bivalent linkers, and nitrate esters)

L61 ANSWER 19 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:157602 HCAPLUS Full-text
DOCUMENT NUMBER: 136:205430
TITLE: Pharmaceutical compositions containing AT-receptor antagonist or insulin secretion enhancers
INVENTOR(S): Allison, Malcolm; Gatlin, Marjorie Regan
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.; Novartis Pharma. GmbH
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002015933	A2	20020228	WO 2001-EP9587	20010820
WO 2002015933	A3	20030814		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001087698	A5	20020304	AU 2001-87698	20010820
EP 1351683	A2	20031015	EP 2001-967289	20010820
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004514654	T	20040520	JP 2002-520854	20010820
US 2004034065	A1	20040219	US 2003-362340	20030616
US 2006089389	A1	20060427	US 2005-295928	20051207
US 2006281790	A1	20061214	US 2006-508353	20060823

PRIORITY APPLN. INFO.:		
US 2000-643641	A	20000822
US 2000-327553P	P	20000822
WO 2001-EP9587	W	20010820
US 2003-362340	B1	20030616
US 2005-295928	B1	20051207

ED Entered STN: 01 Mar 2002
AB A pharmaceutical composition comprises as active ingredients an AT1-receptor antagonist or a salt, an insulin secretion enhancer or a its salt or an insulin sensitizer or its salt. Thus, tablets contained Starlix DS 60,

lactose monohydrate 141.5, microcryst. cellulose 71, Povidone-K30 12, and Croscarmellose sodium 18.4, colloidal SiO2 6.4, Mg stearate 5.7, and Opadry 9 mg.

IC ICM A61K045-00
CC 63-6 (Pharmaceuticals)
IT Angiotensin receptor antagonists
Antianginal agents
Antidiabetic agents
Antihypertensives
Antiobesity agents
Cardiovascular agents
Cataract
Connective tissue, disease
Hyperglycemia
Hypertriglyceridemia
Hypolipemic agents
Skin, disease
(pharmaceutical compns. containing AT-receptor antagonist or insulin secretion enhancers)

IT 339-43-5, Carbutamide 451-71-8, Glyhexamide 535-65-9, Glybuthiazole 631-27-6, Glyclopyramide 664-95-9, Tolcyclamide 968-81-0, Acetohexamide 1156-19-0, Tolazamide 1228-19-9, Glypinamide 1492-02-0, Glybuzole 3149-00-6, Phenbutamide 3459-20-9, Glymidine 4618-41-1, 1-Butyl-3-metanilylurea 9004-10-8, Insulin, biological studies 10238-21-8, Glibenclamide 21187-98-4, Gliclazide 25046-79-1, Glisoxepid 26944-48-9, Glibornuride 29094-61-9, Glipizide 33342-05-1, Gliquidone 93479-97-1, Glimepiride 105816-04-4, Nateglinide 114798-26-4, Losartan 133040-01-4, Eprosartan 135062-02-1, Repaglinide 137862-53-4, Valsartan 138402-11-6, Irbesartan 139481-59-7, Candesartan 144689-63-4, Olmesartan medoxomil 144701-48-4, Telmisartan **145375-43-5, Mitiglinide** 145733-36-4, Tasosartan
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. containing AT-receptor antagonist or insulin secretion enhancers)

L61 ANSWER 20 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:157564 HCAPLUS Full-text
DOCUMENT NUMBER: 136:205424
TITLE: Combinations of insulin secretion enhancer, HMG-CoA **reductase inhibitors** and acetylcholinesterase **inhibitors**
INVENTOR(S): Allison, Malcolm; Gatlin, Marjorie Regan
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.; Novartis Pharma GmbH
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002015892	A2	20020228	WO 2001-EP9586	20010820 <--
WO 2002015892	A3	20030904		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,

PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
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AU 2002014952	A5	20020304	AU 2002-14952	20010820 <--
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JP 2004519424	T	20040702	JP 2002-520813	20010820 <--
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PRIORITY APPLN. INFO.:			US 2000-643642 A	20000822 <--
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ED Entered STN: 01 Mar 2002

AB The present invention relates to a combination, especially a pharmaceutical composition, comprising (a) an insulin secretion enhancer or a pharmaceutically acceptable salt thereof and (b) at least one of the active ingredients selected from the group consisting of (i) HMG-Co-A reductase inhibitors or a pharmaceutically acceptable salt thereof; and (ii) ACE inhibitors or a pharmaceutically acceptable salt thereof; and, in case of a pharmaceutical composition, a pharmaceutically acceptable carrier. Formulations were given as examples, e.g., tablets containing nateglinide.

IC ICM A61K031-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
ST insulin secretion enhancer pharmaceutical combination; HMG CoA **reductase inhibitor** pharmaceutical combination; acetylcholinesterase **inhibitor** pharmaceutical combination
IT Antidiabetic agents
Antihypertensives
Antiobesity agents
Connective tissue, disease
Eye, disease
Hypolipemic agents
Skin, disease
(combinations of insulin secretion enhancer, HMG-CoA **reductase inhibitors** and acetylcholinesterase **inhibitors**)
IT Nerve, disease
(**diabetic** neuropathy; combinations of insulin secretion enhancer, HMG-CoA **reductase inhibitors** and acetylcholinesterase **inhibitors**)
IT Eye, disease
(**diabetic** retinopathy; combinations of insulin secretion enhancer, HMG-CoA **reductase inhibitors** and acetylcholinesterase **inhibitors**)
IT Heart, disease
(failure; combinations of insulin secretion enhancer, HMG-CoA **reductase inhibitors** and acetylcholinesterase **inhibitors**)
IT Kidney, disease
(glomerulosclerosis; combinations of insulin secretion enhancer, HMG-CoA **reductase inhibitors** and acetylcholinesterase **inhibitors**)
IT Sexual disorders
(impotence; combinations of insulin secretion enhancer, HMG-CoA **reductase inhibitors** and acetylcholinesterase **inhibitors**)
IT Eye, disease
(macula, degeneration; combinations of insulin secretion enhancer,

HMG-CoA **reductase inhibitors** and acetylcholinesterase **inhibitors**)

IT Inflammation
Intestine, disease
(ulcerative colitis; combinations of insulin secretion enhancer, HMG-CoA **reductase inhibitors** and acetylcholinesterase **inhibitors**)

IT 9004-10-8, Insulin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(combinations of insulin secretion enhancer, HMG-CoA **reductase inhibitors** and acetylcholinesterase **inhibitors**)

IT 64-77-7, Tolbutamide 94-20-2, Chlorpropamide 339-43-5, Carbutamide 339-44-6, Glymidine 451-71-8, Glyhexamide 535-65-9, Glybuthiazole 631-27-6, Glyclopyramide 664-95-9, Tolcyclamide 968-81-0, Acetohexamide 1156-19-0, Tolazamide 1228-19-9, Glypinamide 1492-02-0, Glybuzole 3149-00-6, Phenbutamide 4618-41-1, 1-Butyl-3-metanilylurea 10238-21-8, Glibenclamide 21187-98-4, Gliclazide 25046-79-1, Glisoxepid 26944-48-9, Glibornuride 29094-61-9, Glipizide 33342-05-1, Gliquidone 62571-86-2, Captopril 74258-86-9, Alacepril 75330-75-5, Lovastatin 75847-73-3, Enalapril 76420-72-9, Enalaprilat 76547-98-3, Lisinopril 79902-63-9, Simvastatin 81093-37-0, Pravastatin 82834-16-0, Perindopril 83435-66-9, Delapril 83647-97-6, Spirapril 85441-61-8, Quinapril 85856-54-8, Moveltipril 86541-75-5, Benazepril 86541-78-8, Benazeprilat 87333-19-5, Ramipril 87679-37-6, Trandolapril 88768-40-5, Cilazapril 89371-37-9, Imidapril 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 98048-97-6, Fosinopril 105816-04-4, Nateglinide 111223-26-8, Ceronapril 111902-57-9, Temocapril 134523-00-5, Atorvastatin 135062-02-1, Repaglinide **145375-43-5, Mitiglinide** 145599-86-6, Cerivastatin 147511-69-1, Pitavastatin 287714-41-4, Rosuvastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combinations of insulin secretion enhancer, HMG-CoA **reductase inhibitors** and acetylcholinesterase **inhibitors**)

IT 9000-81-1, Acetylcholinesterase 9028-35-7, HMG-CoA **reductase**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; combinations of insulin secretion enhancer, HMG-CoA **reductase inhibitors** and acetylcholinesterase **inhibitors**)

L61 ANSWER 21 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:51257 HCAPLUS Full-text
DOCUMENT NUMBER: 136:123595
TITLE: A combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for the treatment of **diabetes**
INVENTOR(S): Van Poelje, Paul D.; Erion, Mark D.; Fujiwara, Toshihiko
PATENT ASSIGNEE(S): Metabasis Therapeutics, Inc., USA; Sankyo Company, Ltd.
SOURCE: PCT Int. Appl., 392 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002003978	A2	20020117	WO 2001-US21557	20010705 <--
WO 2002003978	A3	20031016		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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AU 2001273271	B2	20060105			
US 2003073728	A1	20030417	US 2001-900364		20010705 <--
HU 200301830	A2	20031128	HU 2003-1830		20010705 <--
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
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IN 2002MN01873	A	20050204	IN 2002-MN1873		20021224 <--
ZA 2003000044	A	20040506	ZA 2003-44		20030102 <--
NO 2003000034	A	20030305	NO 2003-34		20030103 <--
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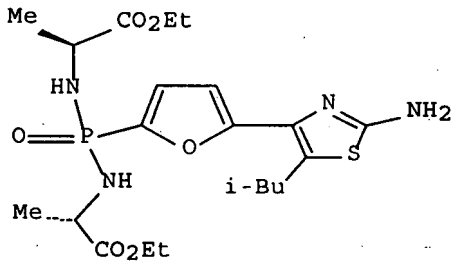
PRIORITY APPLN. INFO.:			US 2000-216531P	P	20000706 <--
			US 2001-900364	A	20010705 <--
			US 2000-215126P	P	20000629 <--
			AU 2001-73271	A3	20010705 <--
			WO 2001-US21557	W	20010705 <--

OTHER SOURCE(S): MARPAT 136:123595

ED Entered STN: 18 Jan 2002

GI



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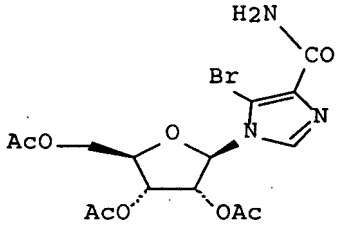


II

AB A combination therapy of at least one FBPase inhibitor ((R1Y)2P(O)M and R14C(O)(CR12R13)nN(R18)P(O)(NR15R16)M; e.g. 2-amino-5-propylthio-4-(5-phosphono-2-furanyl)thiazole monohydrobromide and 2-amino-5-isobutyl-4-[2-[N,N'-bis[(S)-1-(ethoxycarbonyl)ethyl]phosphonodiamido]-5-furanyl]thiazole (shown as I)) and at least one other antidiabetic agent (insulin secretagogue; e.g. glyburide, a sulfonylurea) is disclosed. (R1Y)2P(O)M and R14C(O)(CR12R13)nN(R18)P(O)(NR15R16)M are converted in vivo or in vitro to MPO32-, which inhibit FBPase; the substituents are defined in the claims. General methods and about 15 specific example prepns. of the phosphorus

compds. are included but no methods of preparation are claimed. In the biol. examples, data is presented for the following for selected phosphorus compds. and other materials: inhibition of human liver FBPase, inhibition of rat liver and mouse liver FBPase, inhibition of gluconeogenesis by an FBPase inhibitor in rat hepatocytes, inhibition of glucose production and elevation of fructose-1,6-bisphosphate levels in rat hepatocytes treated with FBPase inhibitors, anal. of hepatic and plasma drug metabolite levels, blood glucose, and hepatic fructose 1,6-bisphosphate levels after administration of compound A (shown as II) p.o. to normal fasted rats, anal. of hepatic and plasma drug levels after administration of compds. i.p. to normal fasted rats, oral bioavailability determination of two compds. and oral glucose lowering activity of two compds. For insulin secretagogues: insulin release from pancreatic islets, glucose lowering in the fasted rat, i.v. glucose tolerance in the fasted rat, oral glucose tolerance in the Zucker diabetic fatty rat, insulin secretion in the rat, inhibition of KATP-channels in mouse pancreatic beta-cells, and sulfonylurea receptor binding. Also included are: inhibition of dipeptidyl peptidase IV (DPP-IV inhibitors), alpha-glucosidase assay, glycogen phosphorylase assay, assay of glucose 6-phosphatase inhibitors, glucagon antagonist assay, amylin agonist assay, fatty acid oxidation inhibitor assay, glucose lowering in the db/db mouse (FBPase inhibitor), glucose lowering in the ZDF rat, acute combination treatment of an insulin secretagogue and an FBPase inhibitor in the ZDF rat, chronic combination treatment of an insulin secretagogue and an FBPase inhibitor in the ZDF rat, acute combination treatment of insulin and an FBPase inhibitor in db/db mice, beneficial effect of chronic combination treatment of insulin and an FBPase inhibitor in db/db mice, and beneficial effect of chronic combination treatment of insulin and an FBPase inhibitor in db/db Mice. Also included are: acute combination treatment of insulin and an FBPase inhibitor in the Goto-Kakizaki rat, acute combination treatment of a biguanide and an FBPase inhibitor in db/db mice, acute combination treatment of an alpha glucosidase inhibitor and an FBPase inhibitor in Goto-Kakizaki rats, acute combination treatment of a glycogen phosphorylase inhibitor and an FBPase inhibitor in db/db or ob/ob mice, acute combination treatment of a glucose-6-phosphatase inhibitor and an FBPase inhibitor in db/db or ob/ob mice, acute combination treatment of an FBPase inhibitor and an amylin agonist, chronic combination treatment of a fatty acid oxidation inhibitor and an FBPase inhibitor in the streptozotocin-induced diabetic rat.

IC ICM A61K031-00

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1, 27, 28, 29

ST antidiabetic agent phosphonate phosphorodiamidate FBPase **inhibitor** **diabetes** treatment; insulin secretagogue phosphonate phosphorodiamidate FBPase **inhibitor** **diabetes** treatment

IT Potassium channel
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ATP-sensitive; combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

IT Glucagon-like peptide-1 receptors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(agonists; combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

IT Sulfonylurea receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(binding; combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

IT Antiobesity agents

(combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful as)

IT Antidiabetic agents
B cell (lymphocyte)
Drug bioavailability
Human
Pancreatic islet of Langerhans
(combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

IT Antioxidants
(fatty acid; combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

IT Liver
(fructose bisphosphatase of; combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

IT Liver
(hepatocyte, fructose bisphosphatase of; combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

IT Gluconeogenesis
(**inhibitors**; combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

IT Fatty acids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

IT Sulfonylureas
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(insulin secretagogues; combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

IT Drug delivery systems
(oral; combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

IT Organic compounds, biological studies
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phosphorus-containing; combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

IT Drug delivery systems
(prodrugs; combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

IT 106602-62-4, Amylin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonists; combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

IT 151126-32-8, Pramlintide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(amylin agonist; combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

IT 9007-92-5, Glucagon, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study) (antagonists; combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

IT 50-99-7, D-Glucose, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study) (blood; combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

IT 213125-12-3P, 5-Diethylphosphono-2-(4-methyl-1-oxopentyl)furan
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

IT 261365-06-4P, 5-Diethylphosphono-2-acetylfuran 261365-08-6P, 5-Diethylphosphono-2-(1-oxobutyl)furan 261365-11-1P, 2-Amino-5-isobutyl-4-[5-phosphono-2-furanyl]thiazole 261365-17-7P 261365-19-9P, 2-Methyl-4-(5-phosphono-2-furanyl)thiazole 261365-23-5P, 2-Isopropyl-4-(5-phosphono-2-furanyl)thiazole 261365-25-7P, 5-Isobutyl-4-(5-phosphono-2-furanyl)thiazole 261365-27-9P, 2-Aminothiocarbonyl-4-(5-phosphono-2-furanyl)thiazole 261365-31-5P 261365-33-7P, 2-(2-Thienyl)-5-isobutyl-4-(5-phosphono-2-furanyl)thiazole 261365-36-0P 261365-37-1P, 2-Acetamido-5-isobutyl-4-(5-phosphono-2-furanyl)thiazole 261365-38-2P, 2-Amino-4-(5-phosphono-2-furanyl)thiazole 261365-40-6P, 2-Methylamino-5-isobutyl-4-(5-phosphono-2-furanyl)thiazole 261365-44-0P 261365-48-4P 261365-51-9P 261365-55-3P 261365-56-4P, 2-Ethoxycarbonyl-4-(5-phosphono-2-furanyl)thiazole 261365-58-6P, 2-Amino-5-ethyl-4-(5-phosphono-2-furanyl)thiazole 261365-60-0P, 2-Cyanomethyl-4-(5-phosphono-2-furanyl)thiazole 261365-62-2P 261365-63-3P, 2-Amino-5-propyl-4-(5-phosphono-2-furanyl)thiazole 261365-65-5P 261365-66-6P, 2-Amino-5-methylthio-4-(5-phosphono-2-furanyl)thiazole 261365-67-7P, 2-Amino-5-cyclopropyl-4-(5-phosphono-2-furanyl)thiazole monohydrobromide 261365-68-8P, 2-Amino-5-cyclopropyl-4-(5-phosphono-2-furanyl)thiazole 261365-70-2P, 2-Amino-5-benzyloxycarbonyl-4-(5-phosphono-2-furanyl)thiazole 261365-72-4P 261365-73-5P, 2-Amino-5-[N,N-dimethylaminomethyl]-4-(5-phosphono-2-furanyl)thiazole dihydrobromide 261365-75-7P, 2-Amino-5-methoxycarbonyl-4-(5-phosphono-2-furanyl)thiazole 261365-78-0P, 2-Amino-5-propyloxycarbonyl-4-(5-phosphono-2-furanyl)thiazole 261365-79-1P, 2-Amino-5-benzyl-4-(5-phosphono-2-furanyl)thiazole 261365-80-4P, 2-Amino-5-[N,N-diethylaminomethyl]-4-(5-phosphono-2-furanyl)thiazole dihydrobromide 261365-83-7P, 2-Amino-5-(N,N-dimethylcarbamoyl)-4-(5-phosphono-2-furanyl)thiazole 261365-85-9P, 2-Amino-5-carboxy-4-(5-phosphono-2-furanyl)thiazole 261365-86-0P, 2-Amino-5-isopropyloxycarbonyl-4-(5-phosphono-2-furanyl)thiazole 261365-89-3P, 2-Methyl-5-cyclopropyl-4-(5-phosphono-2-furanyl)thiazole 261365-90-6P, 2-Methyl-5-ethoxycarbonyl-4-(5-phosphono-2-furanyl)thiazole 261365-92-8P, 2-[N-Acetylamino]-5-methoxymethyl-4-(5-phosphono-2-furanyl)thiazole 261365-95-1P, 2-Amino-5-cyclopropylmethoxycarbonyl-4-(5-phosphono-2-furanyl)thiazole 261365-98-4P, 2-[(N-Dansyl)amino]-5-isobutyl-4-(5-phosphono-2-furanyl)thiazole 261365-99-5P, 2-Amino-5-(2,2,2-trifluoroethyl)-4-(5-phosphono-2-furanyl)thiazole 261366-00-1P, 2-Methyl-5-methylthio-4-(5-phosphono-2-furanyl)thiazole 261366-01-2P, 2-Amino-5-methylthio-4-(5-phosphono-2-furanyl)thiazole

monoammonium salt 261366-02-3P, 2-Cyano-5-ethyl-4-(5-phosphono-2-furanyl)thiazole 261366-03-4P, 2-Amino-5-hydroxymethyl-4-(5-phosphono-2-furanyl)thiazole 261366-05-6P, 2-Cyano-5-isobutyl-4-(5-phosphono-2-furanyl)thiazole 261366-06-7P, 2-Amino-5-isopropylthio-4-(5-phosphono-2-furanyl)thiazole monohydrobromide 261366-07-8P, 2-Amino-5-phenylthio-4-(5-phosphono-2-furanyl)thiazole 261366-08-9P, 2-Amino-5-tert-butylthio-4-(5-phosphono-2-furanyl)thiazole 261366-09-0P, 2-Amino-5-propylthio-4-(5-phosphono-2-furanyl)thiazole monohydrobromide 261366-11-4P, 2-Amino-5-ethylthio-4-(5-phosphono-2-furanyl)thiazole 261366-12-5P, 2-[N-(tert-Butyloxycarbonyl)amino]-5-methoxymethyl-4-(5-phosphono-2-furanyl)thiazole 261366-13-6P, 2-Hydroxy-4-(5-phosphono-2-furanyl)thiazole 261366-14-7P, 2-Hydroxy-5-ethyl-4-(5-phosphono-2-furanyl)thiazole 261366-16-9P, 2-Hydroxy-5-isopropyl-4-(5-phosphono-2-furanyl)thiazole 261366-17-0P, 2-Hydroxy-5-isobutyl-4-(5-phosphono-2-furanyl)thiazole 261366-18-1P, 5-Ethoxycarbonyl-4-(5-phosphono-2-furanyl)thiazole 261366-20-5P, 2-Amino-5-vinyl-4-(5-phosphono-2-furanyl)thiazole 261366-21-6P, 2-Methylthio-5-isobutyl-4-(5-phosphono-2-furanyl)thiazole 261366-24-9P, 2-Amino-5-isobutyl-4-(5-phosphono-2-furanyl)selenazole 261366-26-1P, 2-Amino-5-methylthio-4-(5-phosphono-2-furanyl)selenazole 261366-40-9P, 2-Amino-5-(2-furanyl)-4-(5-phosphono-2-furanyl)thiazole 261366-65-8P, 2-Amino-5-isobutyl-4-(5-phosphono-2-furanyl)oxazole 261366-66-9P, 2-Hydroxy-5-isobutyl-4-(5-phosphono-2-furanyl)imidazole 261366-67-0P, 2-Methyl-4-isobutyl-5-(5-phosphono-2-furanyl)oxazole monohydrobromide 261366-68-1P, 2-Methyl-5-isobutyl-4-(5-phosphono-2-furanyl)oxazole monohydrobromide 261366-69-2P, 2-Methyl-5-isobutyl-4-(5-phosphono-2-furanyl)imidazole monohydrobromide 261366-71-6P, 2-Trifluoromethyl-4-(5-phosphono-2-furanyl)imidazole 261366-73-8P, 4,5-Dimethyl-1-isobutyl-2-(5-phosphono-2-furanyl)imidazole 261366-74-9P, 2-Amino-5-propyl-4-(5-phosphono-2-furanyl)oxazole 261366-75-0P, 2-Amino-5-ethyl-4-(5-phosphono-2-furanyl)oxazole 261366-76-1P, 2-Amino-5-methyl-4-(5-phosphono-2-furanyl)oxazole 261366-77-2P, 2-Amino-4-(5-phosphono-2-furanyl)oxazole 261366-78-3P, 2-Amino-5-isobutyl-4-(5-phosphono-2-furanyl)oxazole monohydrobromide 261370-26-7P 261370-27-8P, 2-Methyl-5-isobutyl-4-(5-phosphorodiamido-2-furanyl)thiazole 261370-29-0P, 2-Amino-5-methylthio-4-(5-phosphorodiamido-2-furanyl)thiazole 261370-30-3P, 2-Amino-5-isobutyl-4-(5-phosphonomonoamido-2-furanyl)thiazole 261370-31-4P, 2-Amino-5-isobutyl-4-(5-phosphorodiamido-2-furanyl)thiazole 261370-32-5P, 2-Amino-5-isobutyl-4-[5-(N,N'-diisobutylphosphorodiamido)-2-furanyl]thiazole 261370-33-6P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(S)-1,3-bis(ethoxycarbonyl)-1-propyl]phosphorodiamido]-2-furanyl]thiazole 261370-34-7P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis((S)-1-benzyloxycarbonylethyl)phosphorodiamido]-2-furanyl]thiazole 261370-35-8P 261370-39-2P, 2-Amino-5-isobutyl-4-[5-[O-phenyl-N-((S)-1-methoxycarbonylethyl)phosphonamido]-2-furanyl]thiazole 261370-44-9P, 2-Amino-5-isobutyl-4-[5-(O-phenylphosphonamido)-2-furanyl]thiazole 261370-46-1P, 2-Amino-5-isobutyl-4-(5-(O-phenyl-N-ethoxycarbonylmethylphosphonamido)-2-furanyl)thiazole 261370-48-3P, 2-Amino-5-isobutyl-4-(5-(O-phenyl-N-isobutylphosphonamido)-2-furanyl)thiazole 261370-50-7P, 2-Amino-5-isobutyl-4-[5-[O-phenyl-N-((S)-1-ethoxycarbonyl-2-phenylethyl)phosphonamido]-2-furanyl]thiazole 261370-54-1P, 2-Amino-5-isobutyl-4-[5-[O-phenyl-N-[(S)-1,3-bis(ethoxycarbonyl)propyl]phosphonamido]-2-furanyl]thiazole 261370-57-4P, 2-Amino-5-isobutyl-4-[5-[O-(3-chlorophenyl)-N-[(S)-1-(methoxycarbonyl)ethyl]phosphonamido]-2-furanyl]thiazole 261370-60-9P, 2-Amino-5-isobutyl-4-[5-[O-phenyl-N-[1,1-bis(ethoxycarbonyl)methyl]phosphonamido]-2-furanyl]thiazole 261370-61-0P, 2-Amino-5-isobutyl-4-[5-[O-phenyl-N-(1-morpholinyl)phosphonamido]-2-furanyl]thiazole 261370-62-1P, 2-Amino-5-isobutyl-4-[5-[O-phenyl-N-[(S)-1-(benzyloxycarbonyl)ethyl]phosphonamido]-2-furanyl]thiazole 261370-63-2P, 2-Amino-5-isobutyl-4-(5-(O-

phenyl-N-benzyloxycarbonylmethylphosphonamido)-2-furanyl)thiazole 261370-64-3P, 2-Amino-5-isobutyl-4-[5-[O-(4-methyloxyphenyl)-N-[(S)-1-(methoxycarbonyl)ethyl]phosphonamido]-2-furanyl]thiazole 261370-68-7P 261370-69-8P 261370-70-1P 261370-71-2P 261370-73-4P 261370-74-5P 261370-76-7P, 2-Amino-5-methylthio-4-(5-(N-methyl-1-phenyl-1,3-propylphosphonamido)-2-furanyl)thiazole 261370-79-0P, 2-Amino-5-isobutyl-4-[5-[[3-(3,5-dichlorophenyl)-1,3-propyl]phosphonamido]-2-furanyl]thiazole 261370-80-3P, 2-Amino-5-isobutyl-4-[5-(4,5-benzo-1-oxo-1-phospha-2-oxa-6-azacyclohexan-1-yl)-2-furanyl]thiazole 261372-35-4P, 2-Amino-4-phosphonomethyloxy-6-bromobenzothiazole 261372-36-5P, 2-Amino-4-phosphonomethyloxybenzothiazole 261372-38-7P, 2-Amino-4-phosphonomethyloxy-6-bromo-7-chlorobenzothiazole 261372-39-8P, 2-Amino-4-phosphonomethoxy-6-bromo-7-methylbenzothiazole 261372-40-1P, 2-Amino-4-phosphonomethoxy-7-methylbenzothiazole 261372-42-3P, 2-Amino-4-phosphonomethoxy-7-chlorobenzothiazole 261372-64-9P, 2-Amino-7-ethyl-6-thiocyano-4-phosphonomethoxybenzothiazole 261373-40-4P, 2-Methyl-5-ethyl-4-(5-phosphono-2-furanyl)thiazole 280779-70-6P, 2-Phenyl-5-isobutyl-4-(5-phosphono-2-furanyl)thiazole 280779-71-7P, 2-Amino-5-isopropyl-4-(5-phosphono-2-furanyl)thiazole 280779-72-8P, 2-Amino-5-methanesulfinyl-4-(5-phosphono-2-furanyl)thiazole 280779-74-0P, 2-Amino-5-(4-morpholinyl)methyl-4-(5-phosphono-2-furanyl)thiazole dihydrobromide 280779-79-5P, 2-Amino-5-ethyl-4-(5-phosphono-2-furanyl)selenazole 280779-91-1P, 2-Vinyl-5-isobutyl-4-(5-phosphono-2-furanyl)thiazole 280782-95-8P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis(benzyloxycarbonylmethyl)phosphonodiamido]furanyl]-2-thiazole 280782-96-9P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(R)-1-(methoxycarbonyl)ethyl]phosphonodiamido]furanyl]-2-thiazole 280782-97-0P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(S)-1-(ethoxycarbonyl)ethyl]phosphonodiamido]furanyl]-2-thiazole 280782-98-1P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(tert-butoxycarbonyl)methyl]phosphonodiamido]furanyl]-2-thiazole 280782-99-2P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(ethoxycarbonyl)methyl]phosphonodiamido]furanyl]-2-thiazole 280783-00-8P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(1-methyl-1-ethoxycarbonyl)ethyl]phosphonodiamido]furanyl]-2-thiazole 280783-01-9P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis(ethoxycarbonylmethyl)-N,N'-dimethylphosphonodiamido]-2-furanyl]thiazole 280783-02-0P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis((S)-1-benzyloxycarbonyl-2-methylpropyl]phosphonodiamido]-2-furanyl]thiazole 280783-03-1P, 2-Amino-5-isobutyl-4-[5-[[N,N'-bis((S)-1-methoxycarbonyl-3-methyl)butyl]phosphonodiamido]-2-furanyl]thiazole 280783-04-2P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(R)-1-ethoxycarbonyl-2-(benzylthio)ethyl]phosphonodiamido]-2-furanyl]thiazole 280783-06-4P, 2-Amino-5-propylthio-4-[5-[N,N'-bis[(S)-1-(ethoxycarbonyl)ethyl]phosphonodiamido]-2-furanyl]thiazole 280783-07-5P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(S)-1-benzyloxycarbonyl-2-methylisobutyl]phosphonodiamido]-2-furanyl]thiazole 280783-08-6P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(S)-1-ethoxycarbonyl-3-methylbutyl]phosphonodiamido]-2-furanyl]thiazole 280783-09-7P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(S)-1-ethoxycarbonyl-2-methylpropyl]phosphonodiamido]-2-furanyl]thiazole 280783-10-0P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis[(S)-1-ethoxycarbonyl-2-phenylethyl]phosphonodiamido]-2-furanyl]thiazole 280783-11-1P, 2-Amino-5-propylthio-4-[5-[N,N'-bis[(1-methyl-1-ethoxycarbonylethyl]phosphonodiamido]-2-furanyl]]thiazole 280783-12-2P, 2-Amino-5-methylthio-4-[5-[N,N'-bis[1-methyl-1-ethoxycarbonylethyl]phosphonodiamido]-2-furanyl]thiazole 280783-13-3P, 2-Amino-5-isobutyl-4-[5-[N-morpholino-N'-[1-methyl-1-ethoxycarbonylethyl]phosphonodiamido]-2-furanyl]thiazole 280783-14-4P, 2-Amino-5-isobutyl-4-[5-[N-pyrrolidino-N'-[1-methyl-1-ethoxycarbonylethyl]phosphonodiamido]-2-furanyl]thiazole 347870-21-7P, 2-Amino-5-isobutyl-4-[5-[N,N'-bis((S)-1-ethoxycarbonylpropyl)phosphorodiam

ido]-2-furanyl]thiazole 347870-33-1P, 2-Amino-5-(2-thienyl)-4-(5-diethylphosphono-2-furanyl)thiazole 358670-36-7P, (5-(3,5-Dinitrophenyl)-2-furanyl)phosphonic acid 358670-37-8P, (5-(2-Amino-3,5-dinitrophenyl)-2-furanyl)phosphonic acid 358670-38-9P, (5-(5-Chloro-2-methoxyphenyl)-2-furanyl)phosphonic acid 358670-39-0P, (5-(2,5-Dichlorophenyl)-2-furanyl)phosphonic acid 358670-40-3P, (5-(2-Methylsulfamoyl-5-(trifluoromethyl)phenyl)-2-furanyl)phosphonic acid 358670-41-4P, (5-(5-Chloro-2-(methylsulfamoyl)phenyl)-2-furanyl)phosphonic acid 358670-42-5P, (5-(2-(Methylsulfamoyl)phenyl)-2-furanyl)phosphonic acid 358670-44-7P, (5-(2-Hydroxyphenyl)-2-furanyl)phosphonic acid 358670-45-8P, (5-(3,5-Dimethylphenyl)-2-furanyl)phosphonic acid 358670-46-9P, (5-(3-Bromophenyl)-2-furanyl)phosphonic acid 358670-47-0P, (5-(4-Aminophenyl)-2-furanyl)phosphonic acid 358670-48-1P, (5-(4-Chloro-2,5-dimethoxyphenyl)-2-furanyl)phosphonic acid 358670-49-2P, (5-(2-((4-Chlorobenzyl)carbamoyl)phenyl)-2-furanyl)phosphonic acid 358670-50-5P, (5-(2-((2-(4-Chlorophenyl)ethyl)carbamoyl)phenyl)-2-furanyl)phosphonic acid 358670-51-6P, (5-(2-(Benzylsulfamoyl)phenyl)-2-furanyl)phosphonic acid 358670-52-7P, (5-(2-Sulfamoylphenyl)-2-furanyl)phosphonic acid 358670-53-8P, (5-Pentamethylphenyl-2-furanyl)phosphonic acid 358670-54-9P, (5-(2,3-Dicarboethoxyphenyl)-2-furanyl)phosphonic acid 358670-56-1P, (5-(4-Acetylamino-3-methylphenyl)-2-furanyl)phosphonic acid 358670-58-3P, (5-(2,4-Dichloro-6-methylphenyl)-2-furanyl)phosphonic acid 358670-59-4P, (5-(4-Hydroxy-2-carbomethoxyphenyl)-2-furanyl)phosphonic acid 358670-60-7P, (5-(2-Carbamoyl-4-methylphenyl)-2-furanyl)phosphonic acid 358670-61-8P, (5-(2-Ethoxycarbonyl-4-hydroxyphenyl)-2-furanyl)phosphonic acid 358670-62-9P, (5-(4-Nitrophenyl)-2-furanyl)phosphonic acid 358670-63-0P, (5-(2-((2,4-Difluorophenyl)carbamoyl)phenyl)-2-furanyl)phosphonic acid 358670-64-1P, (5-(3,5-Dichlorophenyl)-2-furanyl)phosphonic acid 358670-65-2P, (5-(3-Hydroxyphenyl)-2-furanyl)phosphonic acid 358670-66-3P, (5-(5-Bromo-3-carboxyphenyl)-2-furanyl)phosphonic acid 358670-67-4P, (5-(5-Formyl-2,3-dimethoxyphenyl)-2-furanyl)phosphonic acid 358670-68-5P, (5-(2-Nitrophenyl)-2-furanyl)phosphonic acid 358670-69-6P, (5-(Biphenyl-2-yl)-2-furanyl)phosphonic acid 358670-70-9P, (5-(2-(Carboethoxy)phenyl)-2-furanyl)phosphonic acid 358670-71-0P, (5-(4-Bromophenyl)-2-furanyl)phosphonic acid 358670-72-1P, (5-(3-Propanoylphenyl)-2-furanyl)phosphonic acid 358670-73-2P, (5-(5-Cyano-2-methoxyphenyl)-2-furanyl)phosphonic acid 358670-74-3P, (5-(2-Ethylphenyl)-2-furanyl)phosphonic acid 358670-75-4P, (5-(6-Methyl-2-nitrophenyl)-2-furanyl)phosphonic acid 358670-76-5P, (5-(4-(Acetylamino)phenyl)-2-furanyl)phosphonic acid 358670-77-6P, (5-(2,3,4,5-Tetramethylphenyl)-2-furanyl)phosphonic acid 358670-78-7P, (5-(Biphenyl-3-yl)-2-furanyl)phosphonic acid 358670-79-8P, (5-(5-Chloro-2-sulfamoylphenyl)-2-furanyl)phosphonic acid 358670-80-1P, (5-(4-(((1-Pyrrolidinyl)acetyl)amino)phenyl)-2-furanyl)phosphonic acid 358670-81-2P, (5-(3,4-Dimethylphenyl)-2-furanyl)phosphonic acid 358670-82-3P, (5-(2,4-Dinitrophenyl)-2-furanyl)phosphonic acid 358670-83-4P, (5-(3-(Aminomethyl)phenyl)-2-furanyl)phosphonic acid 358670-84-5P, (5-(4-Amino-3-fluorophenyl)-2-furanyl)phosphonic acid 358670-85-6P, (5-(3-(Hydroxymethyl)phenyl)-2-furanyl)phosphonic acid 358670-86-7P, (5-(2-Bromophenyl)-2-furanyl)phosphonic acid 358670-87-8P, (5-(2-(2-Hydroxyethyl)phenyl)-2-furanyl)phosphonic acid 358670-88-9P, (5-(4-Carbamoylphenyl)-2-furanyl)phosphonic acid 358670-89-0P, (5-(4-Cyanophenyl)-2-furanyl)phosphonic acid 358670-90-3P, (5-(3-Cyanophenyl)-2-furanyl)phosphonic acid 358670-91-4P, (5-(2-Cyanophenyl)-2-furanyl)phosphonic acid 358670-92-5P, (5-(4-Amino-3-nitrophenyl)-2-furanyl)phosphonic acid 358670-93-6P, (5-(2-Isopropylphenyl)-2-furanyl)phosphonic acid 358670-94-7P, (5-(6-Amino-2-chloro-3-pyridyl)-2-furanyl)phosphonic acid 358670-95-8P,

(5-(2-Amino-5-chlorophenyl)-2-furanyl)phosphonic acid 358670-96-9P, (5-(3-Chloro-5-fluorophenyl)-2-furanyl)phosphonic acid 358670-97-0P, (5-(2-Methyl-5-nitrophenyl)-2-furanyl)phosphonic acid 358670-98-1P, (5-(5-Fluoro-3-nitrophenyl)-2-furanyl)phosphonic acid 358670-99-2P, (5-(2-Amino-5-carbomethoxyphenyl)-2-furanyl)phosphonic acid 358671-00-8P, (5-(2-Methoxy-5-nitrophenyl)-2-furanyl)phosphonic acid 358671-01-9P, (5-(2-Chloro-5-(trifluoromethyl)phenyl)-2-furanyl)phosphonic acid 358671-02-0P, (5-(2,5-Bis(trifluoromethyl)phenyl)-2-furanyl)phosphonic acid 358671-03-1P, (5-(4-Fluorophenyl)-2-furanyl)phosphonic acid 358671-04-2P, (5-(2,4-Dichlorophenyl)-2-furanyl)phosphonic acid 358671-05-3P, (5-(3-Amino-5-carbomethoxyphenyl)-2-furanyl)phosphonic acid 358671-06-4P, (5-(3-Amino-4-bromophenyl)-2-furanyl)phosphonic acid 358672-11-4P, (5-(4-Methyl-3-thienyl)-2-furanyl)phosphonic acid 389057-32-3P, (5-(2-(Propylsulfamoyl)phenyl)-2-furanyl)phosphonic acid 389057-53-8P 389057-54-9P, 2-Amino-5-ethylthiocarbonyl-4-(5-phosphono-2-furanyl)thiazole 389057-55-0P, 2-Amino-5-methylthio-4-(5-phosphono-2-furanyl)thiazole N,N-dicyclohexylammonium salt 389057-73-2P, 2-Amino-5-isobutyl-4-[5-[O-(4-chlorophenyl)-N-((S)-1-methoxycarbonylethyl)phosphonamido]-2-furanyl]thiazole 389057-74-3P, 2-Amino-5-isobutyl-4-[5-[O-phenyl-N-[2-(ethoxycarbonyl)propyl]phosphonamido]-2-furanyl]thiazole 389057-76-5P, 2-Amino-4-[[3-(3,5-dichlorophenyl)propane-1,3-diyl]phosphonomethoxy]-6,7,8,9-tetrahydronaphtho[1,2-d]thiazole
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

IT 213124-93-7 213199-10-1 213247-37-1 240434-61-1 280783-15-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

IT 213190-65-9, Exendin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(exendin and exendin agonists, insulin secretagogue; combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

IT 9004-10-8, Insulin, biological studies 116094-23-6, Insulin aspart 133107-64-9, Insulin lispro 160337-95-1, Insulin glargine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in combination with phosphonate or phosphorodiamidate FBPase **inhibitors** useful for treatment of **diabetes**)

IT 9001-39-2, Glucose-6-phosphatase 9001-42-7, α-Glucosidase 9001-52-9, Fructose bisphosphatase 9035-74-9, Glycogen phosphorylase 54249-88-6, Dipeptidyl peptidase-IV
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

IT 64-77-7, Tolbutamide 94-20-2, Chlorpropamide 114-86-3, Phenformin 451-71-8, Glyhexamide 657-24-9, Metformin 664-95-9, Tolcyclamide 692-13-7, Buformin 968-81-0, Acetohexamide 1156-19-0, Tolazamide 3149-00-6, Phenbutamide 10238-21-8, Glyburide 21187-98-4, Gliclazide 25046-79-1, Glisoxepid 26944-48-9, Glibornuride 29094-61-9, Glipizide 33342-05-1, Gliquidone 56180-94-0, Acarbose 72432-03-2, Miglitol

83480-29-9, Voglibose 93479-97-1, Glimepiride 105816-04-4, Nateglinide
135062-02-1, Repaglinide 145375-43-5, **Mitiglinide**
161748-40-9, BTS-67582 204656-20-2, NN 2211 247016-69-9, NVP-DPP728
251572-86-8, P 32/98
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(insulin secretagogue; combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

IT 261373-15-3P, 2-Methyl-5-isobutyl-4-(5-phosphono-2-furanyl)thiazole
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(intermediate; combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

IT 1738-68-7, Benzyl aminoacetate 358672-65-8, 6-Amino-2-chloro-3-bromopyridine
RL: RCT (Reactant); RACT (Reactant or reagent)
(intermediate; combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

IT 36366-55-9P, Diethyl 2-furanylphosphonate 78072-59-0P,
2-(4-Methyl-1-oxopentyl)furan 82619-14-5P, Ethoxycarbonyloxymethyl iodide 104208-14-2P 213124-94-8P, 5-Diethylphosphono-2-furaldehyde
261372-78-5P, 2-Bromo-5-isobutyl-4-(5-diethylphosphono-2-furanyl)thiazole
261373-31-3P, 2-Diethylphosphonomethyloxy-5-bromonitrobenzene
389057-77-6P, 4-Phosphonomethoxy-6,7,8,9-tetrahydronaphtho[1,2-d]thiazole dichloridate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

IT 953-18-4P, (R)-Ethyl 2-amino-3-(benzylthio)propanoate 2666-93-5P,
L-Leucine methyl ester 2743-60-4P, L-Leucine ethyl ester 3081-24-1P,
L-Phenylalanine ethyl ester 13200-60-7P, N-Methylglycine ethyl ester
17431-03-7P, L-Valine ethyl ester 21760-98-5P, L-Valine benzyl ester
154092-64-5P, (S)-Benzyl 2-amino-3,3-dimethylbutanoate
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(reactant; combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

IT 78-81-9, Isobutylamine 88-67-5, 2-Iodobenzoic acid 98-01-1,
2-Furaldehyde, reactions 109-80-8, 1,3-Propanedithiol 110-00-9, Furan
110-70-3, N,N'-Dimethylethylenediamine 354-37-0, Trifluoroacetamidine
431-03-8, 2,3-Butanedione 459-73-4, Glycine ethyl ester 533-58-4,
2-Iodophenol 540-37-4, 4-Iodoaniline 583-55-1, 2-Bromo-1-iodobenzene
589-87-7, 1-Bromo-4-iodobenzene 591-18-4, 1-Bromo-3-iodobenzene
609-73-4, 1-Iodo-2-nitrobenzene 622-50-4, 4-Iodoacetanilide 623-00-7,
4-Bromobenzonitrile 626-02-8, 3-Iodophenol 636-98-6,
1-Iodo-4-nitrobenzene 646-07-1, 4-Methylpentanoic acid 672-57-1,
2-Chloro-1-iodo-5-trifluoromethylbenzene 696-40-2, 3-Iodobenzylamine
709-49-9, 1-Iodo-2,4-dinitrobenzene 814-49-3, Diethyl chlorophosphate
873-38-1, 2-Bromo-4-chloroaniline 875-51-4, 4-Bromo-2-nitroaniline
1074-16-4, 2-Bromophenethyl alcohol 1113-49-1, Ethyl
2-amino-2-methylpropanoate 1115-59-9, L-Alanine ethyl ester, hydrochloride 1459-01-4, 2-Iodoisopropylbenzene 1765-93-1,

4-Fluorophenylboronic acid 1817-73-8, 2-Bromo-4,6-dinitroaniline 2042-37-7, 2-Bromobenzonitrile 2113-51-1, 2-Iodobiphenyl 2113-57-7, 3-Bromobiphenyl 2491-20-5, L-Alanine methyl ester hydrochloride 3032-81-3, 3,5-Dichloroiodobenzene 3082-75-5, L-Alanine ethyl ester 3819-88-3, 3-Nitro-5-fluoro-1-iodobenzene 3853-91-6, 1-Iodo-2,3,4,5,6-pentamethylbenzene 3956-07-8, 4-Iodobenzamide 5197-28-4, 2-Bromo-4-nitroanisole 5464-79-9, 2-Amino-4-methoxybenzothiazole 6456-74-2 6937-34-4, 3-Iodophthalic acid 6948-30-7, 3-Bromo-4,5-dimethoxybenzaldehyde 6952-59-6, 3-Bromobenzonitrile 7051-34-5, Cyclopropanemethyl bromide 7617-93-8, 1-Bromo-2,5-bis(trifluoromethyl)benzene 7745-93-9, 2-Bromo-4-nitrotoluene 13529-27-6, 2-Furaldehyde diethyl acetal 16450-41-2, L-Glutamic acid diethyl ester 17831-01-5, L-Alanine benzyl ester 18282-40-1, 1-Ethyl-2-iodobenzene 19718-49-1, 2-Iodo-4-carbomethoxyaniline 19829-31-3, 3'-Bromopropiophenone 21705-13-5, D-Alanine methyl ester 22445-41-6, 5-Iodo-m-xylene 29632-74-4, 2-Fluoro-4-iodoaniline 29682-41-5, 2,5-Dichloro-1-iodobenzene 30318-99-1, 3-Bromo-4-methylthiophene 31599-61-8, 3,4-Dimethyliodobenzene 33863-76-2, 1-Bromo-3-chloro-5-fluorobenzene 41085-43-2, 2-Bromo-3-nitrotoluene 45644-21-1, 6-Amino-2-chloropyridine 52807-27-9, 4-Chloro-2-iodoanisole 53730-99-7, 2-Iodobenzenesulfonamide 54509-71-6, 2,3,4,5-Tetramethyliodobenzene 57455-06-8, 3-Iodobenzyl alcohol 57772-57-3, 5-Hydroxy-2-iodobenzoic acid 63980-69-8, 1-(2-Methoxy-5-chlorophenyl)thiourea 68716-47-2, 2,4-Dichlorophenylboronic acid 85006-23-1, 3-Aminophenylboronic acid hydrochloride 90064-46-3, 2,5-Dimethoxy-4-iodochlorobenzene 106938-62-9, Diethylphosphonomethyl trifluoromethylsulfonate 117324-09-1, 4-Iodo-2-methylacetanilide 117572-79-9, 3-Bromo-4-methoxybenzonitrile 118486-94-5, 2-Tributylstannylfuran 125259-03-2, N-Methyl-2-iodobenzenesulfonamide 175277-97-1, 3,5-Dichloro-2-iodotoluene 188815-32-9, 3-Bromo-5-iodobenzoic acid 261369-11-3, 2-Amino-5-isobutyl-4-(5-diphenylphosphono-2-furanyl)thiazole 261372-76-3, 2-Amino-5-isobutyl-4-(5-diethylphosphono-2-furanyl)thiazole 261372-77-4, 2-Amino-5-bromo-4-(5-diethylphosphono-2-furanyl)thiazole 261373-39-1, 3-(3,5-Dichlorophenyl)-1,3-propanediol 270086-79-8, N-(4-Iodophenyl)-2-(tetrahydro-1H-pyrrol-1-yl)acetamide 271796-28-2, 4-Chloro-2-iodobenzenesulfonamide 271796-61-3, N-Benzyl-2-iodobenzenesulfonamide 271796-68-0, N-Propyl-4-chloro-2-iodobenzenesulfonamide 273208-13-2, N-Methyl-2-iodo-4-(trifluoromethyl)benzenesulfonamide 273208-16-5, N-Methyl-4-chloro-2-iodobenzenesulfonamide 304644-56-2, N-(4-Chlorobenzyl)-2-iodobenzamide 309253-36-9, 2-Iodo-5-methylbenzamide 347869-08-3, 5-Diethylphosphono-2-(2-bromo-4-methyl-1-oxopentyl)furan 347869-10-7, 5-Diethylphosphono-2-(bromoacetyl)furan 347869-19-6, Diethyl (5-iodo-2-furanyl)phosphonate 349110-34-5, N-(2,4-Difluorophenyl)-2-iodobenzamide 358672-63-6, N-(4-Chlorophenethyl)-2-iodobenzamide 358672-64-7, Methyl 5-hydroxy-2-iodobenzoate 380430-56-8, 3-Amino-5-carbomethoxyphenylboronic acid 389057-75-4, 2-Amino-4-phosphonomethoxy-6,7,8,9-tetrahydronaphtho[1,2-d]thiazole 389057-78-7, 4-Diphenylphosphonomethoxy-6,7,8,9-tetrahydronaphtho[1,2-d]thiazole 389057-79-8, 4-Phenylphosphonomethoxy-6,7,8,9-tetrahydronaphtho-[1,2-d]thiazole 389057-80-1, 4-Phosphonomethoxy-6,7,8,9-tetrahydronaphtho[1,2-d]thiazole

RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; combination of phosphonate or phosphorodiamidate FBPase **inhibitors** and antidiabetic agents useful for treatment of **diabetes**)

L61 ANSWER 22 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:743481 HCAPLUS Full-text

DOCUMENT NUMBER: 138:265470
TITLE: Study of the insulinotropic effect of the novel antihyperglycemic agent KAD-1229 using HIT T15 cells, a hamster's insulinoma cell line
AUTHOR(S): Ichikawa, Kiyoshi; Yamato, Tokuhisa; Tsuji, Atsutoshi; Ojima, Kazuma; Kusama, Hiroshi; Kojima, Masami
CORPORATE SOURCE: Pharmacology Research, Research & Development, Kissei Pharmaceutical Co., Ltd., Hotaka, Nagano, Japan
SOURCE: Arzneimittel-Forschung (2002), 52(8), 605-609
CODEN: ARZNAD; ISSN: 0004-4172
PUBLISHER: Editio Cantor Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 02 Oct 2002
AB The insulinotropic effect of (+)-monocalcium bis [(2S)-2-benzyl-3-(cis-hexahydro-2-isoindolinyl-carbonyl)propionate]dihydrate (CAS **145375-43-5**, KAD-1229) was assessed by comparing it with those of glibenclamide (CAS 10238-21-8), nateglinide (CAS 105816-04-4), and repaglinide (CAS 135062-02-1) using HIT T15 cells, a hamster insulinoma cell line. Although their potencies were different, KAD-1229, glibenclamide, nateglinide, and repaglinide all concentration-dependently and significantly induced insulin release from these cells. Further, each agent displaced the binding of 3H-glibenclamide to the cell membrane and inhibited 86Rb+ efflux from the cells. These results indicate that KAD-1229, glibenclamide, nateglinide, and repaglinide each exert their insulinotropic effect by binding to the glibenclamide binding sites (sulfonylurea receptors) on pancreatic β-cells and closing K+ channels. Diazoxide, a K+ channel opener, and nitrendipine, a Ca2+ blocker, suppressed the insulin release induced by KAD-1229 or glibenclamide. These results demonstrate that the insulinotropic actions of KAD-1229 and glibenclamide involve similar underlying pathways.
CC 1-10 (Pharmacology)
ST antihyperglycemic KAD1229 insulinotrope pancreas beta cell **diabetes** mellitus; nateglinide repaglinide glibenclamide hypoglycemic KAD1229 **diabetes**; insulin secretagogue K channel calcium **blocker** sulfonylurea receptor antidiabetic
IT Antidiabetic agents
Diabetes mellitus
(mechanism of antihyperglycemic agent KAD-1229 insulinotropic effect on hamster pancreatic β-cells)
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 23 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:635931 HCAPLUS Full-text
DOCUMENT NUMBER: 135:185506
TITLE: Antidiabetic agents containing α-glucosidase **inhibitors** and insulin secretion promoters
INVENTOR(S): Sugiyama, Yasuo; Odaka, Hiroyuki; Sakiyama, Hiroshi; Iwasaki, Masato; Funatsu, Masami
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2001062295	A1	20010830	WO 2001-JP1282	20010222 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2401356	A1	20010830	CA 2001-2401356	20010222 <--
AU 2001034114	A5	20010903	AU 2001-34114	20010222 <--
EP 1295609	A1	20030326	EP 2001-906193	20010222 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2001316293	A	20011113	JP 2001-47695	20010223 <--
US 2003040490	A1	20030227	US 2002-204783	20020821 <--
PRIORITY APPLN. INFO.:			JP 2000-52297 A	20000224 <--
			WO 2001-JP1282 W	20010222 <--

ED Entered STN: 31 Aug 2001

AB Drugs containing, as the active ingredients, exclusively a combination of an α-glucosidase inhibitor with a non-sulfonylurea insulin secretion promoter, are useful as preventives and remedies for diabetes, etc. Diabetic patients were administered with a tablet containing 0.2 mg voglibose and a tablet containing 2 mg repaglinide before breakfast and blood samples were taken 1 h after meals and the results showed a significant decrease in blood glucose levels.

IC ICM A61K045-06
ICS A61K031-44; A61K031-405; A61K031-198; A61K031-702; A61K031-133; A61K031-70; A61P003-10; A61P043-00

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

ST antidiabetic glucosidase **inhibitor** insulin secretion promoter; voglibose repaglinide **diabetes** control

IT Antidiabetic agents
(antidiabetic agents containing α-glucosidase **inhibitors** and insulin secretion promoters)

IT Drug delivery systems
(tablets; antidiabetic agents containing α-glucosidase **inhibitors** and insulin secretion promoters)

IT 56180-94-0, Acarbose 72432-03-2, Miglitol 80879-63-6, Emiglitate 83480-29-9, Voglibose 105816-04-4, Nateglinide 135062-02-1, Repaglinide **145375-43-5, Mitiglinide**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antidiabetic agents containing α-glucosidase **inhibitors** and insulin secretion promoters)

IT 9001-42-7, α-Glucosidase 9004-10-8, Insulin, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(antidiabetic agents containing α-glucosidase **inhibitors** and insulin secretion promoters)

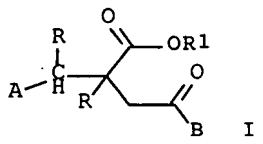
IT 50-99-7, D-Glucose, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(blood; antidiabetic agents containing α-glucosidase **inhibitors** and insulin secretion promoters)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 24 OF 49 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:814308 HCAPLUS Full-text
DOCUMENT NUMBER: 133:359230
TITLE: Use of succinic acid derivatives to obtain a medicine for treating inflammation
INVENTOR(S): Caille, Dominique
PATENT ASSIGNEE(S): Sanofi-Synthelabo, Fr.
SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000067752	A1	20001116	WO 2000-FR1246	20000509 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2793411	A1	20001117	FR 1999-5978	19990511 <--
FR 2793411	B1	20010629		
EP 1178794	A1	20020213	EP 2000-927322	20000509 <--
EP 1178794	B1	20050907		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002544163	T	20021224	JP 2000-616778	20000509 <--
AT 303807	T	20050915	AT 2000-927322	20000509 <--
PRIORITY APPLN. INFO.:			FR 1999-5978 A	19990511 <--
			WO 2000-FR1246 W	20000509 <--

OTHER SOURCE(S): MARPAT 133:359230
ED Entered STN: 21 Nov 2000
GI



I

AB The invention concerns the use of succinic acid derivs. of general formula (I) wherein: A represents a Ph group optionally substituted by one, two or three substituents selected among a halogen, a C1-6 alkyl, C1-6 alkoxy group; a Ph, furyl, pyridyl or cycloalkyl with 3 to 8 carbon atoms; B represents an aminobicyclic group which consists of an amino cyclic compound with 5 or 6 members condensed with a cycloalkyl ring with 5 or 6 members which may have 1 or 2 unsatd. bonds, provided that B is bound to the carbon atom of the

carbonyl group on the nitrogen atom; each R represents a hydrogen atom and all the R radicals are combined together to form a chemical bond; R1 represents a hydrogen atom, a C1-6 alkyl group, an aralkyl group with 7 to 10 carbon atoms; when there exist geometric isomers, each geometric isomer, the isomers E and the isomers Z thereof, the isomers trans and the isomers cis, for treating inflammation. The compns. are administered at a daily dose of 1-100 mg orally, or 0.1-100 mg parenterally (no data).

IC ICM A61K031-4035
ICS A61P029-00

CC 1-7 (Pharmacology)

ST succinic acid deriv inflammation **inhibitor**

IT Nerve, disease
(**diabetic** neuropathy; use of succinic acid derivs. to obtain medicine for treating inflammation)

IT Arthritis
(polyarthritis, **inhibitors**; use of succinic acid derivs. to obtain medicine for treating inflammation)

IT 110-15-6D, Succinic acid, derivs. **145375-43-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of succinic acid derivs. to obtain medicine for treating inflammation)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l61 25-49 ibib ab ind

L61 ANSWER 25 OF 49 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2005331235 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15981944
TITLE: Pharmacology of the meglitinide analogs: new treatment options for type 2 **diabetes** mellitus.
AUTHOR: Malaisse Willy J
CORPORATE SOURCE: Laboratory of Experimental Hormonology, Brussels Free University, Brussels, Belgium.. malaisse@ulb.ac.be
SOURCE: Treatments in endocrinology, **(2003)** Vol. 2, No. 6, pp. 401-14. Ref: 83
Journal code: 101132977. ISSN: 1175-6349.
PUB. COUNTRY: New Zealand
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200507
ENTRY DATE: Entered STN: 29 Jun 2005
Last Updated on STN: 13 Jul 2005
Entered Medline: 12 Jul 2005

AB The expression meglitinide analogs was introduced in 1995 to cover new molecules proposed as non-sulfonylurea insulinotropic agents and displaying structural analogy with meglitinide, such as repaglinide, nateglinide, and **mitiglinide**. Meglitinide analogs display, as judged by conformation analysis, a U-shaped configuration similar to that of antihyperglycemic sulfonylureas such as glibenclamide (glyburide) and glimepiride. In rat pancreatic islets incubated in the presence of 7.0 mmol/L D-glucose, repaglinide and **mitiglinide** demonstrate comparable concentration-response relationships for stimulation of insulin release, with a threshold value < 10 nmol/L and a maximal secretory response at about 10 nmol/L. Several findings indicate that meglitinide analogs provoke the closing of adenosine triphosphate-sensitive potassium

channels, with subsequent gating of voltage-sensitive calcium channels. The effects of meglitinide analogs upon the binding of [3H]glibenclamide to islet cells membranes reinforces this concept. At variance, however, with other meglitinide analogs, the ionic and secretory response to repaglinide (10 micromol/L) is not rapidly reversible in perifused rat islets. In experiments conducted in vivo in control and **diabetic** rats, repaglinide provokes a greater and more rapid increase in plasma insulin concentration and an earlier fall in glycemia than glibenclamide or glimepiride. Onset of effect is also more rapid and duration of effect shorter with nateglinide versus glibenclamide. In clinical studies, single or repeated daily administration of repaglinide increased plasma insulin concentration in a dose-dependent manner, with an incremental peak reached about 2 hours after repaglinide intake. Plasma concentrations of repaglinide are about 5.0 microg/L 2-2.5 hours after oral intake of the drug. Despite the slow reversibility of repaglinide action in vitro, this drug offers advantages over glibenclamide in terms of the possible occurrence of hypoglycemia if a meal is missed. In volunteers receiving a single oral dose of nateglinide (120mg) 10 minutes before a standardized 800 Kcal breakfast, the plasma insulin concentration was higher 5, 10, and 20 minutes after meal intake than when they received a single dose of repaglinide (0.5 or 2.0mg) or placebo 10 minutes before breakfast. Peak plasma concentrations of nateglinide were reached within 2 hours in most volunteers. Peak plasma concentrations of **mitiglinide** were reached 30 minutes after a single oral dose in a representative volunteer. **Mitiglinide** significantly **suppressed** meal-induced elevations in blood glucose concentrations in a study of patients with type 2 **diabetes.** In conclusion, two obvious differences among these meglitinide analogs should be underlined. First, on a molar basis, nateglinide is somewhat less potent than repaglinide or **mitiglinide**, as an insulinotropic agent. The maximal secretory responses evoked by these three meglitinide analogs are, however, identical to one another. Secondly, and as already mentioned, the functional effects of nateglinide and **mitiglinide** are more rapidly reversible than those of repaglinide, for instance in perifused rat islets. The meglitinide analogs offer the advantage over the long-acting antihyperglycemic sulfonylurea glibenclamide of minimizing the risk of undesirable hypoglycemia.

CT Animals
*Benzamides: TU, therapeutic use
*Carbamates: TU, therapeutic use
*Cyclohexanes: TU, therapeutic use
***Diabetes Mellitus, Type 2: DT, drug therapy**
Humans
*Hypoglycemic Agents: TU, therapeutic use
*Phenylalanine: AA, analogs & derivatives
*Phenylalanine: TU, therapeutic use
*Piperidines: TU, therapeutic use

RN 105816-04-4 (nateglinide); 135062-02-1 (repaglinide); 54870-28-9 (meglitinide); 63-91-2 (Phenylalanine)

CN 0 (Benzamides); 0 (Carbamates); 0 (Cyclohexanes); 0 (Hypoglycemic Agents); 0 (Piperidines)

L61 ANSWER 26 OF 49 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2002271275 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12010187
TITLE: Effect of KAD-1229, a novel hypoglycaemic agent, on plasma glucose levels after meal load in type 2 **diabetic** rats.
AUTHOR: Ichikawa Kiyoshi; Yamato Tokuhisa; Ojima Kazuma; Tsuji Atsutoshi; Ishikawa Kohtaro; Kusama Hiroshi; Kojima Masami
CORPORATE SOURCE: Pharmacology Laboratories, Kissei Pharmaceutical Co. Ltd, Hotaka, Nagano, Japan.. kiyoshi_ichikawa@pharm.kissei.co.jp
SOURCE: Clinical and experimental pharmacology & physiology,

(2002 May-Jun) Vol. 29, No. 5-6, pp. 423-7.
Journal code: 0425076. ISSN: 0305-1870.
PUB. COUNTRY: Australia
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 16 May 2002
Last Updated on STN: 30 Aug 2002
Entered Medline: 29 Aug 2002

AB 1. The effects of KAD-1229 (a novel non-sulphonylurea agent), voglibose (an alpha-glucosidase **inhibitor**) and nateglinide (a non-sulphonylurea antihyperglycaemic agent) on hyperglycaemia induced by a meal load were assessed in **diabetic** rats. 2. KAD-1229 **suppressed** the increase in plasma glucose levels seen after a meal load and the area under the curve for plasma glucose levels (AUCglucose) up to 5 h after the meal load. 3. Voglibose also **suppressed** the increase in plasma glucose levels; however, a significant decrease in AUCglucose following voglibose was not observed. 4. Nateglinide **suppressed** the increase in plasma glucose levels at 30 min and 1 h after the meal load; however, plasma glucose levels was above control thereafter and the AUCglucose was not decreased. 5. The results indicate that KAD-1229 has an antihyperglycaemic effect and KAD-1229 is suggested to be a suitable agent for controlling post-prandial hyperglycaemia.

CT Animals
*Blood Glucose: ME, metabolism
Cyclohexanes: PD, pharmacology
Diabetes Mellitus, Experimental: BL, blood
***Diabetes Mellitus, Experimental: DT, drug therapy**
Diabetes Mellitus, Type 2: BL, blood
***Diabetes Mellitus, Type 2: DT, drug therapy**
Food
*Hypoglycemic Agents: PD, pharmacology
*Indoles: PD, pharmacology
*Inositol: AA, analogs & derivatives
Inositol: PD, pharmacology
*Phenylalanine: AA, analogs & derivatives
Phenylalanine: PD, pharmacology
*Postprandial Period
Rats
Rats, Wistar
Species Specificity

RN 105816-04-4 (nateglinide); 63-91-2 (Phenylalanine); 6917-35-7 (Inositol); 83480-29-9 (voglibose)
CN 0 (Blood Glucose); 0 (Cyclohexanes); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (**mitiglinide**)

L61 ANSWER 27 OF 49 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2001260288 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11264248
TITLE: Effects of **mitiglinide** (S 21403) on Kir6.2/SUR1, Kir6.2/SUR2A and Kir6.2/SUR2B types of ATP-sensitive potassium channel.
AUTHOR: Reimann F; Proks P; Ashcroft F M
CORPORATE SOURCE: University Laboratory of Physiology, Parks Road, Oxford OX1 3PT.
SOURCE: British journal of pharmacology, (**2001 Apr**) Vol. 132, No. 7, pp. 1542-8.
Journal code: 7502536. ISSN: 0007-1188.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 21 May 2001
Last Updated on STN: 21 May 2001
Entered Medline: 17 May 2001

AB 1. We have investigated the mechanism of action of the novel anti- **diabetic** agent **mitiglinide** (S 21403) on Kir6.2/SUR1, Kir6.2/SUR2A and Kir6.2/SUR2B types of ATP-sensitive potassium (K(ATP)) channel. These possess a common pore-forming subunit, Kir6.2, and different regulatory sulphonylurea receptor (SUR) subunits. It is believed that they correspond to native K(ATP) channels in pancreatic beta-cells, heart and non-vascular smooth muscle, respectively. 2. Kir6.2 was coexpressed with SUR1, SUR2A or SUR2B in Xenopus oocytes and macroscopic currents were recorded in giant inside-out membrane patches. **Mitiglinide** was added to the intracellular membrane surface. 3. **Mitiglinide** **inhibited** Kir6.2/SUR currents at two sites: a low-affinity site on Kir6.2 and a high-affinity site on SUR. Low-affinity **inhibition** was similar for all three types of K(ATP) channel but high-affinity **inhibition** was greater for Kir6.2/SUR1 currents (IC(50), 4 nM) than for Kir6.2/SUR2A or Kir6.2/SUR2B currents (IC(50), 3 and 5 microM, respectively). 4. **Inhibition** of Kir6.2/SUR1 currents was only slowly reversible on the time scale of electrophysiological experiments. 5. Kir6.2/SUR1-S1237Y currents, which previously have been shown to lack high affinity tolbutamide **inhibition**, resembled Kir6.2/SUR2 currents in being unaffected by 100 nM but **blocked** by 10 microM **mitiglinide**. 6. Our results show that **mitiglinide** is a high-affinity drug that shows a 1000 fold greater affinity for the beta-cell type than the cardiac and smooth muscle types of K(ATP) channel, when measured in excised patches.

CT Check Tags: Female
*Adenosine Triphosphate: PH, physiology
Animals
Dose-Response Relationship, Drug
*Indoles: PD, pharmacology
Membrane Potentials: DE, drug effects
Mice
*Potassium Channels: DE, drug effects
Potassium Channels: GE, genetics
Potassium Channels: PH, physiology
*Potassium Channels, Inwardly Rectifying
Protein Subunits
RNA, Messenger: AD, administration & dosage
RNA, Messenger: GE, genetics
Xenopus laevis

RN 56-65-5 (Adenosine Triphosphate)

CN 0 (Indoles); 0 (Potassium Channels); 0 (Potassium Channels, Inwardly Rectifying); 0 (Protein Subunits); 0 (RNA, Messenger); 0 (**mitiglinide**)

L61 ANSWER 28 OF 49 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2001689244 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11716850
TITLE: The effects of **mitiglinide** (KAD-1229), a new anti-**diabetic** drug, on ATP-sensitive K+ channels and insulin secretion: comparison with the sulfonylureas and nateglinide.
AUTHOR: Sunaga Y; Gonoi T; Shibasaki T; Ichikawa K; Kusama H; Yano H; Seino S
CORPORATE SOURCE: Department of Cellular and Molecular Medicine, Graduate School of Medicine, Chiba University 1-8-1 Inohana, Chuo-ku, 260-8670, Chiba, Japan.

SOURCE: European journal of pharmacology, (2001 Nov 9)
Vol. 431, No. 1, pp. 119-25.
Journal code: 1254354. ISSN: 0014-2999.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 11 Dec 2001
Last Updated on STN: 25 Jan 2002
Entered Medline: 11 Jan 2002

AB Mitiglinide (KAD-1229), a new anti-diabetic drug, is thought to stimulate insulin secretion by closing the ATP-sensitive K+ (K(ATP)) channels in pancreatic beta-cells. However, its selectivity for the various K(ATP) channels is not known. In this study, we examined the effects of mitiglinide on various cloned K(ATP) channels (Kir6.2/SUR1, Kir6.2/SUR2A, and Kir6.2/SUR2B) reconstituted in COS-1 cells, and compared them to another meglitinide-related compound, nateglinide. Patch-clamp analysis using inside-out recording configuration showed that mitiglinide inhibits the Kir6.2/SUR1 channel currents in a dose-dependent manner (IC50 value, 100 nM) but does not significantly inhibit either Kir6.2/SUR2A or Kir6.2/SUR2B channel currents even at high doses (more than 10 microM). Nateglinide inhibits Kir6.2/SUR1 and Kir6.2/SUR2B channels at 100 nM, and inhibits Kir6.2/SUR2A channels at high concentrations (1 microM). Binding experiments on mitiglinide, nateglinide, and repaglinide to SUR1 expressed in COS-1 cells revealed that they inhibit the binding of [3H]glibenclamide to SUR1 (IC50 values: mitiglinide, 280 nM; nateglinide, 8 microM; repaglinide, 1.6 microM), suggesting that they all share a glibenclamide binding site. The insulin responses to glucose, mitiglinide, tolbutamide, and glibenclamide in MIN6 cells after chronic mitiglinide, nateglinide, or repaglinide treatment were comparable to those after chronic tolbutamide and glibenclamide treatment. These results indicate that, similar to the sulfonylureas, mitiglinide is highly specific to the Kir6.2/SUR1 complex, i.e., the pancreatic beta-cell K(ATP) channel, and suggest that mitiglinide may be a clinically useful anti-diabetic drug.

CT *ATP-Binding Cassette Transporters
Animals
COS Cells
Cell Line
Cyclohexanes: PD, pharmacology
Glyburide: PD, pharmacology
*Hypoglycemic Agents: PD, pharmacology
*Indoles: PD, pharmacology
*Insulin: ME, metabolism
Patch-Clamp Techniques
*Phenylalanine: AA, analogs & derivatives
Phenylalanine: PD, pharmacology
Potassium Channels: GE, genetics
*Potassium Channels: ME, metabolism
*Potassium Channels, Inwardly Rectifying
Receptors, Drug: GE, genetics
Receptors, Drug: ME, metabolism
Sulfonylurea Compounds: PD, pharmacology
Tolbutamide: PD, pharmacology
Transfection
RN 10238-21-8 (Glyburide); 105816-04-4 (nateglinide); 11061-68-0 (Insulin); 63-91-2 (Phenylalanine); 64-77-7 (Tolbutamide)
CN 0 (ATP-Binding Cassette Transporters); 0 (Cyclohexanes); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (Potassium Channels); 0 (Potassium Channels,

Inwardly Rectifying); 0 (Receptors, Drug); 0 (Sulfonylurea Compounds); 0 (**mitiglinide**); 0 (sulfonylurea receptor)

L61 ANSWER 29 OF 49 MEDLINE on STN
ACCESSION NUMBER: 2006653767 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 17087304
TITLE: Glinide(s), sulfonylurea(s).
AUTHOR: Arakawa Masayuki; Hirose Takahisa
CORPORATE SOURCE: Department of Medicine, Metabolism and Endocrinology, Juntendo University School of Medicine.
SOURCE: Nippon rinsho. Japanese journal of clinical medicine, (2006 Nov) Vol. 64, No. 11, pp. 2107-12. Ref: 16
Journal code: 0420546. ISSN: 0047-1852.
PUB. COUNTRY: Japan
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200701
ENTRY DATE: Entered STN: 8 Nov 2006
Last Updated on STN: 10 Jan 2007
Entered Medline: 9 Jan 2007

AB **Diabetic** macroangiopathy has already developed before diagnosis of **diabetes** mellitus. **Postprandial hyperglycemia** has been known as a risk factor for **diabetic** macroangiopathy and may be more powerful than fasting **hyperglycemia**. To intervene in **hyperglycemia**, insulin secretagogues, glinides which selectively stimulate early meal-induced insulin secretion and improve **postprandial hyperglycemia** , and sulfonylureas which enhance total daily insulin secretion and improve fasting **hyperglycemia**, have been prescribed as major oral antidiabetic agents. Few evidences that amelioration of glycemic control with insulin secretagogues lower the risk of cardiovascular diseases have been reported. But current studies have shown that intervention in **postprandial hyperglycemia** with drugs including glinides decreased thickness of carotid IMT as a surrogate marker of atherosclerosis. Results from on-going large scale intervention study with glinides may clarify whether amelioration of **hyperglycemia** lower the risk of atherosclerotic events.

CT Arteriosclerosis: ET, etiology
***Arteriosclerosis: PC, prevention & control**
Cardiovascular Diseases: ET, etiology
***Cardiovascular Diseases: PC, prevention & control**
*Cyclohexanes: TU, therapeutic use
Diabetic Angiopathies: ET, etiology
***Diabetic Angiopathies: PC, prevention & control**
Glucose Intolerance: CO, complications
Glucose Intolerance: DT, drug therapy
Hyperglycemia: CO, complications
***Hyperglycemia: DT, drug therapy**
Hyperglycemia: PP, physiopathology
*Hypoglycemic Agents: TU, therapeutic use
*Indoles: TU, therapeutic use
Insulin: SE, secretion
*Phenylalanine: AA, analogs & derivatives
Phenylalanine: TU, therapeutic use
Postprandial Period
Risk Factors
*Sulfonylurea Compounds: TU, therapeutic use

RN 105816-04-4 (nateglinide); 11061-68-0 (Insulin); 63-91-2 (Phenylalanine)
CN 0 (Cyclohexanes); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (Sulfonylurea Compounds); 0 (**mitiglinide**)

L61 ANSWER 30 OF 49 MEDLINE on STN
ACCESSION NUMBER: 2005676318 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16363700
TITLE: Significance of insulin secretion pattern lectured by "glinides" in the treatment of **postprandial hyperglycemia.**
AUTHOR: Hirose Takahisa
CORPORATE SOURCE: Department of Medicine, Metabolism and Endocrinology, Juntendo University School of Medicine.
SOURCE: Nippon rinsho. Japanese journal of clinical medicine, (2005 Dec) Vol. 63, No. 12, pp. 2237-44. Ref: 14
Journal code: 0420546. ISSN: 0047-1852.
PUB. COUNTRY: Japan
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200603
ENTRY DATE: Entered STN: 22 Dec 2005
Last Updated on STN: 11 Mar 2006
Entered Medline: 10 Mar 2006

AB The mechanisms by which **postprandial hyperglycemia** is elicited were discussed through therapies of type 2 **diabetes** using "glinides". It has been believed that the earliest determinant of progression to type 2 **diabetes** is a loss of early insulin secretion, a defect which results in **postprandial hyperglycemia** and is often believed to reflect insulin resistance. To prove that, we improved insulin secretion pattern without increase of total amount of insulin secretion using glinide and assessed glucose response. Glinide which selectively enhances early meal-induced insulin secretion improved **postprandial hyperglycemia**, could provide a valuable treatment option in the **prevention** and treatment of type 2 **diabetes.**

CT *Cyclohexanes: TU, therapeutic use
Diabetes Mellitus, Type 2: CO, complications
Eating
Humans
***Hyperglycemia: DT, drug therapy**
Hyperglycemia: ET, etiology
*Hypoglycemic Agents: TU, therapeutic use
*Indoles: TU, therapeutic use
*Insulin: SE, secretion
*Phenylalanine: AA, analogs & derivatives
Phenylalanine: TU, therapeutic use

RN 105816-04-4 (nateglinide); 11061-68-0 (Insulin); 63-91-2 (Phenylalanine)
CN 0 (Cyclohexanes); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (**mitiglinide**)

L61 ANSWER 31 OF 49 MEDLINE on STN
ACCESSION NUMBER: 2005147537 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15779420
TITLE: Effects of **mitiglinide** in treatment of impaired glucose tolerance.
AUTHOR: Katahira Hiroshi; Ishida Hitoshi
CORPORATE SOURCE: Third Department of Internal Medicine, Kyorin University School of Medicine.
SOURCE: Nippon rinsho. Japanese journal of clinical medicine, (2005 Feb) Vol. 63 Suppl 2, pp. 444-50. Ref: 15
Journal code: 0420546. ISSN: 0047-1852.
PUB. COUNTRY: Japan

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200506
ENTRY DATE: Entered STN: 23 Mar 2005
Last Updated on STN: 15 Jun 2005
Entered Medline: 14 Jun 2005
CT Adenosine Triphosphate: ME, metabolism
Animals
Diabetes Mellitus, Type 2: ET, etiology
Diabetes Mellitus, Type 2: PC, prevention & control
Humans
Hyperglycemia: CO, complications
***Hyperglycemia: DT, drug therapy**
Hypoglycemic Agents: PK, pharmacokinetics
***Hypoglycemic Agents: PD, pharmacology**
***Hypoglycemic Agents: TU, therapeutic use**
Indoles: PK, pharmacokinetics
***Indoles: PD, pharmacology**
***Indoles: TU, therapeutic use**
***Insulin: SE, secretion**
Postprandial Period
Potassium Channels: DE, drug effects
Stimulation, Chemical
RN 11061-68-0 (Insulin); 56-65-5 (Adenosine Triphosphate)
CN 0 (Hypoglycemic Agents); 0 (Indoles); 0 (Potassium Channels); 0 (**mitiglinide**)

L61 ANSWER 32 OF 49 MEDLINE on STN
ACCESSION NUMBER: 2005147534 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15779417
TITLE: Selection of oral antidiabetic drugs.
AUTHOR: Iwamoto Yasuhiko
CORPORATE SOURCE: Diabetes Center, Tokyo Women's Medical University.
SOURCE: Nippon rinsho. Japanese journal of clinical medicine, (2005 Feb) Vol. 63 Suppl 2, pp. 428-32. Ref: 9
Journal code: 0420546. ISSN: 0047-1852.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200506
ENTRY DATE: Entered STN: 23 Mar 2005
Last Updated on STN: 15 Jun 2005
Entered Medline: 14 Jun 2005
CT Acarbose
Administration, Oral
Biguanides
Cardiovascular Diseases: ET, etiology
Cardiovascular Diseases: PC, prevention & control
Diabetes Mellitus, Type 2: ET, etiology
Diabetes Mellitus, Type 2: PC, prevention & control
Enzyme Inhibitors
Glucose Intolerance: CO, complications
Glucose Intolerance: DT, drug therapy
Humans
***Hypoglycemic Agents**
Hypoglycemic Agents: AD, administration & dosage

Hypoglycemic Agents: AE, adverse effects
Hypoglycemic Agents: CL, classification
Hypoglycemic Agents: PD, pharmacology
Indoles
Risk
Sulfonylurea Compounds
Thiazolidinediones
alpha-Glucosidases: AI, antagonists & inhibitors
RN 2295-31-0 (2,4-thiazolidinedione); 56180-94-0 (Acarbose)
CN 0 (Biguanides); 0 (Enzyme **Inhibitors**); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (Sulfonylurea Compounds); 0 (Thiazolidinediones); 0 (**mitiglinide**); EC 3.2.1.20 (alpha-Glucosidases)

L61 ANSWER 33 OF 49 MEDLINE on STN
ACCESSION NUMBER: 2004624721 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15561904
TITLE: The impact of ATP-sensitive K+ channel subtype selectivity of insulin secretagogues for the coronary vasculature and the myocardium.
AUTHOR: Quast Ulrich; Stephan Damian; Bieger Susanne; Russ Ulrich
CORPORATE SOURCE: Department of Pharmacology and Toxicology, Medical Faculty, University of Tubingen, Wilhelmstrasse. 56, D-72074 Tubingen, Germany.. ulrich.quast@uni-tuebingen.de
SOURCE: Diabetes, (2004 Dec) Vol. 53 Suppl 3, pp. S156-64. Ref: 58
Journal code: 0372763. ISSN: 0012-1797.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200504
ENTRY DATE: Entered STN: 20 Dec 2004
Last Updated on STN: 15 Apr 2005
Entered Medline: 14 Apr 2005

AB Insulin secretagogues (sulfonylureas and glinides) increase insulin secretion by closing the ATP-sensitive K+ channel (KATP channel) in the pancreatic beta-cell membrane. KATP channels subserve important functions also in the heart. First, KATP channels in coronary myocytes contribute to the control of coronary blood flow at rest and in hypoxia. Second, KATP channels in the sarcolemma of cardiomyocytes (sarcKATP channels) are required for adaptation of the heart to stress. In addition, the opening of sarcKATP channels and of KATP channels in the inner membrane of mitochondria (mitoKATP channels) plays a central role in ischemic preconditioning. Opening of sarcKATP channels also underlies the ST-segment elevation of the electrocardiogram, the primary diagnostic tool for initiation of lysis therapy in acute myocardial infarction. Therefore, **inhibition** of cardiovascular KATP channels by insulin secretagogues is considered to increase cardiovascular risk. Electrophysiological experiments have shown that the secretagogues differ in their selectivity for the pancreatic over the cardiovascular KATP channels, being either highly selective (approximately 1,000x; short sulfonylureas such as nateglinide and **mitiglinide**), moderately selective (10-20x; long sulfonylureas such as glibenclamide [glyburide]), or essentially nonselective (<2x; repaglinide). New binding studies presented here give broadly similar results. In clinical studies, these differences are not yet taken into account. The hypothesis that the in vitro selectivity of the insulin secretagogues is of importance for the cardiovascular outcome of **diabetic** patients with coronary artery disease needs to be tested.

CT *Adenosine Triphosphate: PH, physiology
Animals

*Coronary Circulation: PH, physiology
*Heart: PH, physiology
Humans
*Hypoglycemic Agents: PD, pharmacology
*Insulin: SE, secretion
Models, Molecular
Potassium Channels, Inwardly Rectifying: CH, chemistry
Potassium Channels, Inwardly Rectifying: DE, drug effects
*Potassium Channels, Inwardly Rectifying: PH, physiology
Protein Conformation
Protein Subunits: CH, chemistry
Sulfonylurea Compounds: PD, pharmacology
RN 11061-68-0 (Insulin); 56-65-5 (Adenosine Triphosphate)
CN 0 (Hypoglycemic Agents); 0 (Kir6.2 channel); 0 (Potassium Channels, Inwardly Rectifying); 0 (Protein Subunits); 0 (Sulfonylurea Compounds)

L61 ANSWER 34 OF 49 MEDLINE on STN
ACCESSION NUMBER: 2004390172 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15293870
TITLE: **Mitiglinide**: KAD 1229, S 21403.
AUTHOR: Anonymous
SOURCE: Drugs in R&D, (2004) Vol. 5, No. 2, pp. 98-101. Ref: 13
Journal code: 100883647. ISSN: 1174-5886.
PUB. COUNTRY: New Zealand
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 6 Aug 2004
Last Updated on STN: 4 Feb 2005
Entered Medline: 3 Feb 2005

AB **Mitiglinide** [KAD 1229, S 21403], a derivative of benzylsuccinic acid, is a potassium channel antagonist undergoing development with Kissei for the treatment of type 2 **diabetes** mellitus. It has potent oral hypoglycaemic activity and is structurally different from the sulphonylureas, although it stimulates calcium influx by binding to the suphonylurea receptor on pancreatic beta-cells and closing K+ATP channels. **Mitiglinide** belongs to a family of meglitinide analogues that also includes repaglinide and nateglinide. **Mitiglinide** is licensed to Servier for Europe, where it is undergoing phase III development, and for Russia, the Commonwealth of Independent States, the Baltic Republics, the Middle East, Oceania, China (including Hong Kong) and Taiwan. Kissei exclusively licensed **mitiglinide** to Choongwae Pharma for South Korea in March 2003. In August 2002, Kissei and Takeda entered into a co-marketing agreement for **mitiglinide** in Japan. The companies will co-market the agent under a single brand name. **Mitiglinide** was licensed to Purdue Pharma for the US, Canada, Mexico and Central and South America. However, Kissei and Purdue Pharma terminated their agreement in February 2001 following Purdue Pharma's decision to concentrate on core areas such as oncology and analgesics. Kissei's US subsidiary, Kissei Pharma US, is currently carrying on the ongoing phase II clinical development in the US. However, in its Annual Report 2003, Kissei announced that it is considering outlicensing **mitiglinide** for development in marketing in North America. **Mitiglinide** has been recommended for approval in Japan for the management of postprandial hyperglycaemia in patients with type 2 **diabetes**. Kissei is also conducting phase II/III clinical trials with a combination of **mitiglinide** and an alpha-glucosidase **inhibitor** (additional indication) in patients with type 2 **diabetes** in Japan. In the US, the agent is being evaluated in phase II clinical trials with Kissei Pharma USA. **Mitiglinide** is also undergoing a phase-III, 12-month, multicentre, randomised, double-blind study in a total of

710 patients in comparison with repaglinide for the treatment of type 2 **diabetes**. This study will be followed by a 12-month open-label treatment with **mitiglinide** alone or in combination therapy. Servier (Australia) conducted a randomised, double-blind, multicentre phase III study in Australia comparing **mitiglinide** with metformin or a combination of the two for the treatment of type 2 **diabetes**.

CT Animals
Diabetes Mellitus, Type 2: DT, drug therapy
Humans
Hypoglycemic Agents: PD, pharmacology
*Hypoglycemic Agents: TU, therapeutic use
Indoles: PD, pharmacology
*Indoles: TU, therapeutic use
Randomized Controlled Trials

CN 0 (Hypoglycemic Agents); 0 (Indoles); 0 (**mitiglinide**)

L61 ANSWER 35 OF 49 MEDLINE on STN
ACCESSION NUMBER: 2003345780 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12877090
TITLE: Nateglinide and **mitiglinide**.
AUTHOR: Odawara Masato
CORPORATE SOURCE: Department of Endocrinology and Metabolism, Toranomon Hospital.
SOURCE: Nippon rinsho. Japanese journal of clinical medicine, **(2003 Jul)** Vol. 61, No. 7, pp. 1230-7. Ref: 12
Journal code: 0420546. ISSN: 0047-1852.
PUB. COUNTRY: Japan
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 25 Jul 2003
Last Updated on STN: 26 Sep 2003
Entered Medline: 25 Sep 2003

AB Patients with type 2 **diabetes** mellitus are associated with insulin resistance and/or impaired insulin secretion. Previous observations indicate that Japanese patients with type 2 **diabetes** tend to have impaired insulin response after glycemic load more often than Caucasian counterparts. Recently it has been reported that **hyperglycemia** after glucose load is itself a risk factor for the development of cardiovascular complications in the absence of elevated fasting plasma glucose. Recent observations on the association of post-challenge or **post-prandial hyperglycemia** with cardiovascular events suggest that lowering post-prandial plasma glucose may protect patients from developing cardiovascular diseases. Results of STOP-NIDDM trial suggest that nateglinide, which attenuates post-prandial glycemic surge in type 2 **diabetes**, may also be helpful for the protection against cardiovascular events. Nateglinide exerts its effects shortly after its administration and the effects continue for only about 3 hours. The patients receiving this agent rarely gain weight and develop hypoglycemia. This agent exerts hypoglycemic effects additively with alpha-gulucosidase **inhibitors** or metformin.

CT Cardiovascular Diseases: ET, etiology
Cardiovascular Diseases: PC, prevention & control
Cyclohexanes: PD, pharmacology
*Cyclohexanes: TU, therapeutic use
Diabetes Mellitus, Type 2: CO, complications
Diabetes Mellitus, Type 2: DT, drug therapy
Drug Therapy, Combination
Humans

Hyperglycemia: CO, complications
*Hyperglycemia: DT, drug therapy
*Hypoglycemic Agents: TU, therapeutic use
Indoles: PD, pharmacology
*Indoles: TU, therapeutic use
*Insulin: SE, secretion
Insulin Resistance
Metformin: TU, therapeutic use
Phenylalanine: AA, analogs & derivatives
Phenylalanine: PD, pharmacology
*Phenylalanine: TU, therapeutic use
Postprandial Period
Stimulation, Chemical
RN 105816-04-4 (nateglinide); 11061-68-0 (Insulin); 63-91-2 (Phenylalanine); 657-24-9 (Metformin)
CN 0 (Cyclohexanes); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (**mitiglinide**)

L61 ANSWER 36 OF 49 MEDLINE on STN
ACCESSION NUMBER: 2002028119 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11472274
TITLE: Rapid acting insulinotropic agents: restoration of early insulin secretion as a physiologic approach to improve glucose control.
AUTHOR: Pratley R E; Foley J E; Dunning B E
CORPORATE SOURCE: Novartis Pharmaceuticals Corporation, 59 Route 10, East Hanover, New Jersey 07936, USA..
richard.pratley@pharma.novartis.com
SOURCE: Current pharmaceutical design, **(2001 Sep)** Vol. 7, No. 14, pp. 1375-97. Ref: 143
Journal code: 9602487. ISSN: 1381-6128.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 21 Jan 2002
Last Updated on STN: 21 Jan 2002
Entered Medline: 4 Dec 2001

AB The loss of early insulin secretion appears to be a critical event in the deterioration in glucose tolerance during the development of type 2 **diabetes.** There is therefore a strong rationale for developing new antidiabetic agents aimed at restoring or replacing early prandial insulin secretion and thereby curbing mealtime glucose excursions in patients with type 2 **diabetes.** Four such new agents are either now available (repaglinide and nateglinide) or in clinical development (KAD-1229 and BTS 67 582). Preclinical studies suggest that each of these new insulinotropic agents share a common receptor/effector mechanism with the sulfonylureas (SUs) but that each may have distinct characteristics that differentiate them from the SUs and from each other. Nateglinide and KAD-1229 clearly stimulate biphasic insulin secretion in vitro and in vivo and their effects are rapidly reversible, whereas the effects of repaglinide and BTS 67 582 are prolonged well beyond their removal from perfusion media in vitro or their clearance in vivo. Available data from human studies indicate that the pharmacokinetics of repaglinide and nateglinide are similar, i.e., they are both rapidly absorbed and **eliminated,** but consistent with findings from animal studies, the insulinotropic and glucose-lowering effects of repaglinide are slower in onset and more prolonged than those of nateglinide. Repaglinide and nateglinide have been shown to be safe and well-tolerated in patients with type 2 **diabetes** and to produce

clinically-meaningful **reductions** of HbA1c, both alone and in combination with agents with complementary modes of action (e.g., metformin and thiazolidinediones). Because these new agents can potentially bring patients to near normoglycemia without an undue risk of hypoglycemia, they are important additions to the therapeutic armamentarium.

CT Animals
Carbamates: CH, chemistry
Carbamates: PK, pharmacokinetics
Carbamates: TU, therapeutic use
Cyclohexanes: CH, chemistry
Cyclohexanes: PK, pharmacokinetics
Cyclohexanes: TU, therapeutic use
***Diabetes Mellitus, Type 2: BL, blood**
***Diabetes Mellitus, Type 2: DT, drug therapy**
*Glucose: ME, metabolism
Guanidines: CH, chemistry
Guanidines: PK, pharmacokinetics
Guanidines: TU, therapeutic use
Humans
Hypoglycemic Agents: CH, chemistry
Hypoglycemic Agents: PK, pharmacokinetics
*Hypoglycemic Agents: TU, therapeutic use
Indoles: CH, chemistry
Indoles: PK, pharmacokinetics
Indoles: TU, therapeutic use
Insulin: BL, blood
Insulin: PH, physiology
*Insulin: SE, secretion
*Phenylalanine: AA, analogs & derivatives
Phenylalanine: CH, chemistry
Phenylalanine: PK, pharmacokinetics
Phenylalanine: TU, therapeutic use
Piperidines: CH, chemistry
Piperidines: PK, pharmacokinetics
Piperidines: TU, therapeutic use

RN 105816-04-4 (nateglinide); 11061-68-0 (Insulin); 135062-02-1 (repaglinide); 50-99-7 (Glucose); 63-91-2 (Phenylalanine)

CN 0 (BTS 67582); 0 (Carbamates); 0 (Cyclohexanes); 0 (Guanidines); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (Piperidines); 0 (**mitiglinide**)

L61 ANSWER 37 OF 49 MEDLINE on STN

ACCESSION NUMBER: 2001301378 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11174074
TITLE: Effect of KAD-1229, a nonsulfonylurea hypoglycemic agent, on plasma glucose and insulin in streptozotocin-induced **diabetic** dogs.
AUTHOR: Misawa K; Ichikawa K; Ojima K; Hamano S; Kitamura T; Komatsu H
CORPORATE SOURCE: Pharmacological Laboratories, Kissei Pharmaceutical Co. Ltd., Hotaka, Nagano, Japan.. keiko_misawa@pharm.kissei.co.jp
SOURCE: Pharmacology, **(2001 Feb)** Vol. 62, No. 2, pp. 65-72.
Journal code: 0152016. ISSN: 0031-7012.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105

ENTRY DATE: Entered STN: 4 Jun 2001
Last Updated on STN: 4 Jun 2001
Entered Medline: 31 May 2001

AB Hypoglycemic agents with a rapid onset and short duration of action should be useful for controlling **postprandial hyperglycemia.** Our aim was to establish a **diabetes** mellitus model in dogs, and then during an oral glucose tolerance test to compare the hypoglycemic effect and insulinotropic action of KAD-1229, a new hypoglycemic agent, with that of gliclazide, a conventional sulfonylurea. In this model, KAD-1229 **reduced** the increase in plasma glucose level without producing hypoglycemia. Gliclazide had a weaker effect on **reduction** of the glucose increase and caused hypoglycemia via a significantly raised insulin secretion in the late phase. A rapid insulinotropic action of KAD-1229 was clearly observed in the portal venous blood. The results suggest that in type 2 **diabetes** caused by, at least, insulin deficiency, KAD-1229 may improve impaired insulin secretion in the early phase and attenuate **hyperglycemia** without causing a sustained hypoglycemia. Copyright 2001 S. Karger AG, Basel.

CT Check Tags: Male
Animals
Anti-Bacterial Agents
*Blood Glucose: DE, drug effects
***Diabetes Mellitus, Experimental: BL, blood**
Disease Models, Animal
Dogs
Gliclazide: PD, pharmacology
Glucose Tolerance Test
*Hypoglycemic Agents: PD, pharmacology
*Indoles: PD, pharmacology
*Insulin: BL, blood
Streptozocin

RN 11061-68-0 (Insulin); 18883-66-4 (Streptozocin); 21187-98-4 (Gliclazide)

CN 0 (Anti-Bacterial Agents); 0 (Blood Glucose); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (**mitiglinide**)

L61 ANSWER 38 OF 49 MEDLINE on STN
ACCESSION NUMBER: 1999215370 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 10199157
TITLE: Non-SU, insulin secretagogues.
AUTHOR: Kikuchi M
CORPORATE SOURCE: Institute for Adult Diseases, Asahi Life Foundation.
SOURCE: Nippon rinsho. Japanese journal of clinical medicine, **(1999 Mar)** Vol. 57, No. 3, pp. 702-8. Ref: 21
Journal code: 0420546. ISSN: 0047-1852.
PUB. COUNTRY: Japan
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 1 Jun 1999
Last Updated on STN: 1 Jun 1999
Entered Medline: 18 May 1999

AB The chemical structures, mechanisms of actions, bioavailabilities, insulinotrophic and hypoglycemic actions, and clinical trials of three novel oral hypoglycemic agents, NN-623, A-4166 and KAD-1229 are overviewed. They are non-SU insulin secretagogues and they induce quicker and shorter hypoglycemia than sulphonylureas do, presumably because they are rapidly absorbed into (Tmax: < 30 min) and excreted from blood (T 1/2: < 60 min). They bind to the SU-receptors and **suppress** K-ATP channels like sulphonylureas

do. They stimulate mainly the initial phase of insulin release and evoke a decrease in postprandial rises in plasma glucose in several animals and humans. Clinical trials demonstrated they are efficacious and safe in the treatment of NIDDM subjects. They are useful as a first choice drug for the early stage of NIDDM.

CT *Cyclohexanes: TU, therapeutic use
***Diabetes Mellitus, Type 2: DT, drug therapy**
Humans
*Hypoglycemic Agents: TU, therapeutic use
*Indoles: TU, therapeutic use
*Phenylalanine: AA, analogs & derivatives
Phenylalanine: TU, therapeutic use

RN 105816-04-4 (nateglinide); 63-91-2 (Phenylalanine)

CN 0 (Cyclohexanes); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (**mitiglinide**)

L61 ANSWER 39 OF 49 MEDLINE on STN

ACCESSION NUMBER: 1999410611 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 10479476
TITLE: Effect of the meglitinide analog S21403 on cationic fluxes and insulin release in perifused rat pancreatic islets exposed to a high concentration of D-glucose.
AUTHOR: Louchami K; Jijakli H; Malaisse W J
CORPORATE SOURCE: Laboratory of Experimental Medicine, Brussels Free University, 808 Route de Lennik, Brussels, B-1070, Belgium.
SOURCE: Pharmacological research : the official journal of the Italian Pharmacological Society, **(1999 Sep)** Vol. 40, No. 3, pp. 297-300.
Journal code: 8907422. ISSN: 1043-6618.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 11 Jan 2000
Last Updated on STN: 11 Jan 2000
Entered Medline: 1 Nov 1999

AB The effect of the meglitinide analog S21403 (10 microm) upon(86)Rb and(45)Ca outflow and insulin release was investigated in perifused rat islets exposed to a high concentration of D-glucose (16.7 mm) in order to simulate the situation found in **diabetic** patients. Under these conditions, S21403 provoked a rapid, sustained and rapidly reversible increase in(86)Rb outflow, (45)Ca efflux and insulin release. These effects were **suppressed** or reversed when the experiments were conducted in the absence of extracellular Ca2+. They support the view that S21043 could be used as a novel insulinotropic tool in the treatment of non-insulin-dependent **diabetes** mellitus, the cationic and secretory responses to the drug displaying a favourable time course for prompt and not unduly prolonged activation of islet B-cells. Copyright 1999 Academic Press.

CT Check Tags: Female
Animals
Calcium: ME, metabolism
*Calcium: PK, pharmacokinetics
Calcium Radioisotopes
Cations
*Glucose: PD, pharmacology
*Hypoglycemic Agents: PD, pharmacology
*Indoles: PD, pharmacology
*Insulin: SE, secretion

*Islets of Langerhans: DE, drug effects
*Islets of Langerhans: ME, metabolism
Islets of Langerhans: SE, secretion
Perfusion
Rats
Rats, Wistar
*Rubidium: PK, pharmacokinetics
Rubidium Radioisotopes
RN 11061-68-0 (Insulin); 50-99-7 (Glucose); 7440-17-7 (Rubidium); 7440-70-2 (Calcium)
CN 0 (Calcium Radioisotopes); 0 (Cations); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (Rubidium Radioisotopes); 0 (**mitiglinide**)

L61 ANSWER 40 OF 49 MEDLINE on STN
ACCESSION NUMBER: 2000280282 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 10820647
TITLE: Recent developments and emerging therapies for type 2 **diabetes** mellitus.
AUTHOR: Evans A J; Krentz A J
CORPORATE SOURCE: Department of Diabetes and Endocrinology, Southampton General Hospital, England.
SOURCE: Drugs in R&D, **(1999 Aug)** Vol. 2, No. 2, pp. 75-94. Ref: 106
Journal code: 100883647. ISSN: 1174-5886.
PUB. COUNTRY: New Zealand
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 11 Aug 2000
Last Updated on STN: 11 Aug 2000
Entered Medline: 1 Aug 2000

AB Most patients with type 2 (non-insulin-dependent) **diabetes** mellitus require pharmacotherapy, initially as monotherapy and subsequently in combination, as adjuncts to diet and exercise. Exogenous insulin is ultimately required in a substantial proportion, reflecting the progressive natural history of the disease. Sulphonylureas and biguanides have been employed for over 4 decades as oral antidiabetic agents, but they have a limited capacity to provide long term glycaemic control and can cause serious adverse effects. Thus, more efficacious and tolerable antidiabetic agents are required. Recent years have witnessed the introduction of agents with novel modes of action, that is, the alpha-glucosidase **inhibitors** acarbose and miglitol (which **reduce** postprandial hyperglycaemia) and the first of the thiazolidinedione insulinsensitising drugs--troglitazone and rosiglitazone. Although the former has been withdrawn in some countries due to adverse effects, another 'glitazone' pioglitazone is expected to be approved in the near future. Other recently introduced drugs include glimepiride and the meglitinide insulin secretagogue, repaglinide. Attention is also focusing increasingly on combination therapy using insulin together with sulphonylureas, metformin or troglitazone. Rapid-acting insulin analogues are now being used as alternatives to conventional insulins; their role in the management of type 2 **diabetes** mellitus is presently uncertain but reports of a **reduced** frequency of hypoglycaemia are encouraging. The development of new drugs aims to counter the principal metabolic defects of the disorder, respectively, relative insulin deficiency and insulin resistance. Novel classes of rapid-acting secretagogues under evaluation include the morphilinoguanide BTS 67582 and the meglitinides **mitiglinide** (KAD 1229) and senaglinide (A-4166). Succinate ester derivatives represent a potential novel approach to improving beta-cell function through enhancement of insulin biosynthesis and secretion. Enhancement of nutrient-induced insulin

secretion is a mechanism with several putative targets within the beta-cell; potentiators of insulin secretion include glucagon-like peptide-1 and its analogues, phosphodiesterase **inhibitors** and the imidazoline derivative PMS 812 (S 21663). The amylin agonist pramlintide slows gastric emptying and **suppression** of glucagon secretion. Non-thiazolidinedione insulin-sensitising agents include the gamma-receptor agonist G 1262570X (GG 570) and D-chiro-inositol. Insulin analogues with prolonged action and inhaled insulin preparations are also under investigation. Insulin-mimetic agents include organic vanadium compounds. Whether newer agents will offer clinically relevant efficacy and tolerability advantages over existing therapies remains to be determined.

CT **Diabetes Mellitus, Type 2: DH, diet therapy**
***Diabetes Mellitus, Type 2: DT, drug therapy**
Humans
Hypoglycemic Agents: AE, adverse effects
Hypoglycemic Agents: CL, classification
Hypoglycemic Agents: PD, pharmacology
*Hypoglycemic Agents: TU, therapeutic use

CN 0 (Hypoglycemic Agents)

L61 ANSWER 41 OF 49 MEDLINE on STN
ACCESSION NUMBER: 97041658 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8886929
TITLE: A rapid- and short-acting hypoglycemic agent KAD-1229 improves **post-prandial** **hyperglycemia** and **diabetic** complications in streptozotocin-induced non-insulin-dependent **diabetes** mellitus rats.
AUTHOR: Ohnota H; Kitamura T; Kinukawa M; Hamano S; Shibata N; Miyata H; Ujiie A
CORPORATE SOURCE: Central Research Laboratories, Kissei Pharmaceutical Co., Ltd., Nagano, Japan.
SOURCE: Japanese journal of pharmacology, **(1996 Aug)** Vol. 71, No. 4, pp. 315-23.
Journal code: 2983305R. ISSN: 0021-5198.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19 Feb 1997
Last Updated on STN: 19 Feb 1997
Entered Medline: 30 Jan 1997

AB We investigated therapeutic effects of a rapid- and short-acting non-sulfonylurea hypoglycemic agent, calcium (2S)-2-benzyl-3-(cis- hexahydro-2-isoindolinylcarbonyl)propionate dihydrate (KAD-1229), on streptozotocin (STZ)-induced non-insulin-dependent **diabetes** mellitus (NIDDM) rats. The effects exerted by KAD-1229 on the post-prandial plasma glucose rise in STZ-induced mild NIDDM (mNIDDM) rats were different from those of sulfonylureas. When KAD-1229 with liquid meal (10 kcal/kg) was given to the mNIDDM rats, the plasma glucose migration was similar to that of normal healthy rats. On the contrary, glibenclamide had little or no effect on the plasma glucose rise 0.5-1 hr after oral administration, and its effect was only evident 2-5 hr after dosing. Tolbutamide showed similar hypoglycemia to that induced by glibenclamide at 2-5 hr with insufficient efficacy at 0.5 hr. Gliclazide sufficiently **suppressed** the level of post-prandial plasma glucose. However, its complete **inhibition** of post-prandial plasma glucose was associated with the extra-hypoglycemia 1-5 hr after oral administration. We also tested the efficacy of KAD-1229 in more severe STZ-induced NIDDM (sNIDDM) rats to elucidate the effects of the drug on the long-term glycemic controls and

diabetic complications. When the sNIDDM rats were treated with 10 mg/kg KAD-1229 twice a day for about 17 weeks, increases in fasting plasma glucose and hemoglobin A1c were **inhibited**. Furthermore, treatment with KAD-1229 **suppressed** the development of microalbuminuria and cortical cataract. We conclude that the rapid- and short-acting insulinotropic agent KAD-1229 is able to improve the deterioration in the glycemic controls and **inhibit** the development of **diabetic** complications in STZ-induced NIDDM rats.

CT Check Tags: Male
Albuminuria: ME, metabolism
Analysis of Variance
Animals
Blood Glucose: ME, metabolism
Diabetes Mellitus, Experimental: BL, blood
***Diabetes Mellitus, Experimental: DT, drug therapy**
Glucagon: BL, blood
Hyperglycemia: DT, drug therapy
*Hypoglycemic Agents: PD, pharmacology
*Indoles: PD, pharmacology
Insulin: BL, blood
Pancreas: CH, chemistry
Pancreas: EN, enzymology
Rats
Rats, Sprague-Dawley
Streptozocin

RN 11061-68-0 (Insulin); 18883-66-4 (Streptozocin); 9007-92-5 (Glucagon)

CN 0 (Blood Glucose); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (**mitiglinide**)

L61 ANSWER 42 OF 49 MEDLINE on STN

ACCESSION NUMBER: 95323823 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 7600439

TITLE: Normalization of impaired glucose tolerance by the short-acting hypoglycemic agent calcium (2S)-2-benzyl-3-(cis-hexahydro-2-isoindolinylcarbonyl)propionate dihydrate (KAD-1229) in non-insulin-dependent **diabetes** mellitus rats.

AUTHOR: Ohnota H; Koizumi T; Kobayashi M; Momose Y; Sato F

CORPORATE SOURCE: Creative Products Research Laboratory, Kissei Pharmaceutical Co., Ltd., Nagano-ken, Japan.

SOURCE: Canadian journal of physiology and pharmacology, (**1995 Jan**) Vol. 73, No. 1, pp. 1-6.
Journal code: 0372712. ISSN: 0008-4212.

PUB. COUNTRY: Canada

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199508

ENTRY DATE: Entered STN: 22 Aug 1995
Last Updated on STN: 22 Aug 1995
Entered Medline: 7 Aug 1995

AB We have investigated the hypoglycemic effects of the newly synthesized short-acting nonsulphonylurea hypoglycemic agent calcium (2S)-2-benzyl-3-(cis-hexahydro-2-isoindolinylcarbonyl)-propionate dihydrate (KAD-1229) in non-insulin-dependent **diabetes** mellitus (NIDDM) rats. NIDDM rats that were given a neonatal injection of 60 mg/kg streptozotocin showed a dose-dependent but attenuated response to oral administration of KAD-1229 and gliclazide, and their impaired glucose tolerance was improved but not normalized. We next produced, using a neonatal injection of 30 mg/kg streptozotocin, a mild type of NIDDM rat with less impaired glucose tolerance. These rats responded well to these insulinotropic hypoglycemic agents. Their impaired glucose and meal

tolerance were completely normalized by oral administration of 3 mg/kg KAD-1229. The efficacy of KAD-1229 in this NIDDM rat model 1-3 h after oral glucose administration was comparable with similar doses of gliclazide, despite its shorter hypoglycemic action (compared with gliclazide), in fasting normal rats. In meal tolerance tests (20 kcal/kg; 1 cal = 4.2 J), KAD-1229 **reduced** abnormally enhanced plasma glucose levels 1-3 h after administration. This effect disappeared by 5 h. In contrast, gliclazide showed sustained hypoglycemic effects until 5 h after oral administration, with a lower postprandial (0.5-1 h) effect. These data indicated that the rapid- and short-acting efficacy of KAD-1229 would be beneficial and sufficient to control postprandial plasma glucose in NIDDM rats.

CT Animals
Animals, Newborn
*Blood Glucose: ME, metabolism
*Diabetes Mellitus, Experimental: BL, blood
Food
Gliclazide: PD, pharmacology
Glucose Tolerance Test
*Hypoglycemic Agents: PD, pharmacology
Immunohistochemistry
*Indoles: PD, pharmacology
Pancreas: ME, metabolism
Rats
Rats, Sprague-Dawley

RN 21187-98-4 (Gliclazide)

CN 0 (Blood Glucose); 0 (Hypoglycemic Agents); 0 (Indoles); 0 (**mitiglinide**)

L61 ANSWER 43 OF 49 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN DUPLICATE 1

ACCESSION NUMBER: 2003324437 EMBASE Full-text
TITLE: Sulphonylurea action revisited: The post-cloning era.
AUTHOR: Gribble F.M.; Reimann F.
CORPORATE SOURCE: Dr. F.M. Gribble, Department of Clinical Biochemistry, Addenbrooke's Hospital, Box 232, Hills Road, Cambridge, CB2 2QR, United Kingdom. fmg23@cam.ac.uk
SOURCE: Diabetologia, (1 Jul 2003) Vol. 46, No. 7, pp. 875-891. .
Refs: 163
ISSN: 0012-186X CODEN: DBTGAJ
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 4 Sep 2003
Last Updated on STN: 4 Sep 2003

AB Hypoglycaemic agents such as sulphonylureas and the newer group of "glinides" stimulate insulin secretion by closing ATP-sensitive potassium (K(ATP)) channels in pancreatic beta cells, but have varying cross-reactivity with related channels in extrapancreatic tissues such as heart, vascular smooth and skeletal muscle. Experiments on the structure-function relationships of recombinant K(ATP) channels and the phenotypes of mice deficient in different K(ATP) channel subunits have provided important insights into the mechanisms underlying sulphonylurea selectivity, and the potential consequences of K(ATP) channel **blockade** outside the pancreatic beta cell. The different pharmacological properties of K(ATP) channels from beta cells compared with

those from cardiac, smooth and skeletal muscle, are accounted for by the expression of alternative types of sulphonylurea receptor, with non-identical drug binding sites. The sulphonylureas and glinides are found to fall into two groups: one exhibiting selectivity for beta cell sulphonylurea receptors (SUR1), and the other **blocking** cardiovascular and skeletal muscle sulphonylurea receptors (SUR2) with potencies similar to their action on SUR1. In seeking potential side effects of K(ATP) channel **inhibitors** in humans, it is essential to take these drug differences into account, along with the probability (suggested by the studies on K(ATP) channel knockout mice) that the effects of extrapancreatic K(ATP) channel **inhibition** might be either subtle or rare. Further studies are still required before a final decision can be made on whether non-selective agents are appropriate for the therapy of Type 2 **diabetes.**

CT Medical Descriptors:
***non insulin dependent diabetes mellitus: DT, drug therapy**
drug mechanism
drug effect
drug receptor binding
insulin release
inwardly rectifying potassium channel
pancreas islet beta cell
cross reaction
heart
vascular smooth muscle
skeletal muscle
phenotype
drug selectivity
protein expression
drug binding site
drug potency
side effect: SI, side effect
knockout mouse
medical decision making
cloning
human
nonhuman
review
priority journal
Drug Descriptors:
*sulfonylurea: AE, adverse drug reaction
*sulfonylurea: IT, drug interaction
*sulfonylurea: DT, drug therapy
*sulfonylurea: PD, pharmacology
tolbutamide: DT, drug therapy
tolbutamide: PD, pharmacology
gliclazide: DT, drug therapy
gliclazide: PD, pharmacology
mitiglinide: DT, drug therapy
mitiglinide: PD, pharmacology
glibenclamide: DT, drug therapy
glibenclamide: PD, pharmacology
glimepiride: DT, drug therapy
glimepiride: PD, pharmacology
repaglinide: DT, drug therapy
repaglinide: PD, pharmacology
insulin: EC, endogenous compound
adenosine triphosphate
sulfonylurea receptor: EC, endogenous compound
receptor subtype: EC, endogenous compound
chlorpropamide: DT, drug therapy

chlorpropamide: PD, pharmacology
meglitinide: DT, drug therapy
meglitinide: PD, pharmacology
nateglinide: DT, drug therapy
nateglinide: PD, pharmacology
diazoxide: IT, drug interaction
diazoxide: PD, pharmacology
nicorandil: DT, drug therapy
nicorandil: PD, pharmacology
pinacidil
cromakalim

RN (tolbutamide) 473-41-6, 64-77-7; (gliclazide) 21187-98-4; (**mitiglinide**) 145525-41-3, **207844-01-7**; (glibenclamide) 10238-21-8; (glimepiride) 93479-97-1; (repaglinide) 135062-02-1; (insulin) 9004-10-8; (adenosine triphosphate) 15237-44-2, 56-65-5, 987-65-5; (chlorpropamide) 94-20-2; (meglitinide) 54870-28-9; (nateglinide) 105746-37-0, 105816-04-4, 105816-06-6; (diazoxide) 364-98-7; (nicorandil) 65141-46-0; (pinacidil) 60560-33-0; (cromakalim) 94470-67-4

L61 ANSWER 44 OF 49 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2003422728 EMBASE Full-text
TITLE: [Current oral agents for type 2 **diabetes**].
TIP 2 DIYABETTE GUNCEL ORAL AJANLAR.
AUTHOR: Stoller W.A.
SOURCE: SENDROM, (2003) Vol. 15, No. 6, pp. 24-33. .
Refs: 22
ISSN: 1016-5134 CODEN: SENDEY
COUNTRY: Turkey
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
017 Public Health, Social Medicine and Epidemiology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: Turkish
SUMMARY LANGUAGE: English; Turkish
ENTRY DATE: Entered STN: 6 Nov 2003
Last Updated on STN: 6 Nov 2003

AB Type 2 **diabetes** has reached epidemic levels in the United States. Progressive evidence has emphasized the importance of glucose control in avoiding the high costs and **reduced** quality of life associated with the numerous complications of **diabetes**. Fortunately, pharmacologic options for treating type 2 **diabetes** have increased dramatically during the last 6 years, allowing new opportunities for successful outcomes. Such options will continue to expand. Therefore we are challenged to effectively use these agents in a logical progressive regimen while minimizing side effects.

CT Medical Descriptors:
***non insulin dependent diabetes mellitus: DT, drug therapy**
***non insulin dependent diabetes mellitus: EP, epidemiology**
United States
quality of life
cost of illness
pathophysiology
hypoglycemia: SI, side effect
meteorism: SI, side effect
anorexia: SI, side effect
side effect: SI, side effect
human
review
Drug Descriptors:

*oral antidiabetic agent: AE, adverse drug reaction
*oral antidiabetic agent: DT, drug therapy
*oral antidiabetic agent: PO, oral drug administration
sulfonylurea: AE, adverse drug reaction
sulfonylurea: DT, drug therapy
sulfonylurea: PO, oral drug administration
glibenclamide: DT, drug therapy
glibenclamide: PO, oral drug administration
glimepiride: DT, drug therapy
glimepiride: PO, oral drug administration
glipizide: DT, drug therapy
glipizide: PO, oral drug administration
repaglinide: AE, adverse drug reaction
repaglinide: DT, drug therapy
repaglinide: PO, oral drug administration
mitiglinide: DT, drug therapy
mitiglinide: PO, oral drug administration
nateglinide: AE, adverse drug reaction
nateglinide: DT, drug therapy
nateglinide: PO, oral drug administration
alpha glucosidase inhibitor: DT, drug therapy
alpha glucosidase inhibitor: PO, oral drug administration
metformin: AE, adverse drug reaction
metformin: DT, drug therapy
metformin: PO, oral drug administration
insulin: DT, drug therapy
peroxisome proliferator activated receptor agonist: AE, adverse drug reaction
peroxisome proliferator activated receptor agonist: DT, drug therapy
peroxisome proliferator activated receptor agonist: PO, oral drug administration
pioglitazone: DT, drug therapy
pioglitazone: PO, oral drug administration
rosiglitazone: DT, drug therapy
rosiglitazone: PO, oral drug administration
human insulin: DT, drug therapy
insulin glargine: DT, drug therapy
hemoglobin A1c: EC, endogenous compound
acarbose: AE, adverse drug reaction
acarbose: DT, drug therapy
acarbose: PO, oral drug administration
miglitol: AE, adverse drug reaction
miglitol: DT, drug therapy
miglitol: PO, oral drug administration
glibenclamide plus metformin
starfix

RN (glibenclamide) 10238-21-8; (glimepiride) 93479-97-1; (glipizide) 29094-61-9; (repaglinide) 135062-02-1; (**mitiglinide**) 145525-41-3, **207844-01-7**; (nateglinide) 105746-37-0, 105816-04-4, 105816-06-6; (metformin) 1115-70-4, 657-24-9; (insulin) 9004-10-8; (pioglitazone) 105355-27-9, 111025-46-8; (rosiglitazone) 122320-73-4, 155141-29-0; (human insulin) 11061-68-0; (insulin glargine) 160337-95-1; (hemoglobin A1c) 62572-11-6; (acarbose) 56180-94-0; (miglitol) 72432-03-2

CN Humulin; Novolin; Lantus; Glucovance; Prandin; Starfix; Precose; Glyset

L61 ANSWER 45 OF 49 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2004050138 EMBASE Full-text
TITLE: World Congress of Pharmacology - XIVth Annual Meeting: New

drugs I: 7-12 July 2002, San Francisco, CA, USA.

AUTHOR: Waterworth C.; Durrance A.
CORPORATE SOURCE: C. Waterworth, Current Drugs Ltd., Middlesex House, 34-42 Cleveland Street, London W1T 4LB, United Kingdom. charlotte.waterworth@current.drugs.com

SOURCE: IDrugs, (2002) Vol. 5, No. 8, pp. 745-748. .
ISSN: 1369-7056 CODEN: IDRUFN
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 037 Drug Literature Index
029 Clinical Biochemistry
025 Hematology
030 Pharmacology
018 Cardiovascular Diseases and Cardiovascular Surgery
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Feb 2004
Last Updated on STN: 12 Feb 2004

CT Medical Descriptors:
human
clinical trial
nonhuman
protein targeting
thrombocyte aggregation
kidney function
diabetes mellitus
Alzheimer disease
drug potency
drug activity
drug structure
drug dose regimen
thrombosis: DT, drug therapy
atherosclerosis: DT, drug therapy
drug effect
obesity: DT, drug therapy
dose response
area under the curve
cognitive defect: DT, drug therapy
drug metabolism
drug half life
drug bioavailability
drug blood level
glaucoma: DT, drug therapy
tumor: DT, drug therapy
conference paper

CT Drug Descriptors:
*new drug: PD, pharmacology
*new drug: AN, drug analysis
*new drug: DO, drug dose
*new drug: CM, drug comparison
*new drug: DT, drug therapy
*new drug: PO, oral drug administration
*new drug: CT, clinical trial
*new drug: PK, pharmacokinetics
*new drug: CR, drug concentration
purine P2Y receptor: EC, endogenous compound
antithrombocytic agent: PD, pharmacology
antithrombocytic agent: AN, drug analysis
antithrombocytic agent: DO, drug dose
antithrombocytic agent: CM, drug comparison
antithrombocytic agent: DT, drug therapy

dinucleoside polyphosphate inhibitor: PD, pharmacology
dinucleoside polyphosphate inhibitor: AN, drug analysis
dinucleoside polyphosphate inhibitor: DO, drug dose
dinucleoside polyphosphate inhibitor: CM, drug comparison
dinucleoside polyphosphate inhibitor: DT, drug therapy
peroxisome proliferator activated receptor agonist: DT, drug therapy
peroxisome proliferator activated receptor agonist: PD, pharmacology
peroxisome proliferator activated receptor agonist: CM, drug comparison
peroxisome proliferator activated receptor agonist: AN, drug analysis
acetylsalicylic acid 3 (nitroxymethyl)phenyl ester: DT, drug therapy
acetylsalicylic acid 3 (nitroxymethyl)phenyl ester: CM, drug comparison
acetylsalicylic acid 3 (nitroxymethyl)phenyl ester: PD, pharmacology
mitiglinide: DT, drug therapy
mitiglinide: PD, pharmacology
mitiglinide: PK, pharmacokinetics
mitiglinide: DO, drug dose
mitiglinide: AN, drug analysis
peptide derivative: DT, drug therapy
peptide derivative: CT, clinical trial
peptide derivative: PD, pharmacology
peptide derivative: AN, drug analysis
noopept: DT, drug therapy
noopept: CT, clinical trial
noopept: PD, pharmacology
noopept: AN, drug analysis
pirfenidone: DT, drug therapy
pirfenidone: CT, clinical trial
pirfenidone: PK, pharmacokinetics
pirfenidone: IV, intravenous drug administration
pirfenidone: DO, drug dose
pirfenidone: AN, drug analysis
nitronaproxen: DT, drug therapy
nitronaproxen: PK, pharmacokinetics
nitronaproxen: PO, oral drug administration
nitronaproxen: CR, drug concentration
nitronaproxen: PD, pharmacology
nitronaproxen: AN, drug analysis
6 chloro 2 [(1 furo[2,3 c]pyridin 5 ylethyl)thio] 4 pyrimidinamine: DT, drug therapy
6 chloro 2 [(1 furo[2,3 c]pyridin 5 ylethyl)thio] 4 pyrimidinamine: CT, clinical trial
6 chloro 2 [(1 furo[2,3 c]pyridin 5 ylethyl)thio] 4 pyrimidinamine: AN, drug analysis
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: DT, drug therapy
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: PD, pharmacology
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: CT, clinical trial
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: DO, drug dose
2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid: PK, pharmacokinetics
antiglaucoma agent: DT, drug therapy
antiglaucoma agent: CT, clinical trial
antiglaucoma agent: PD, pharmacology
antineoplastic agent: DT, drug therapy
antineoplastic agent: PD, pharmacology
nitrostyrene derivative: DT, drug therapy
nitrostyrene derivative: PD, pharmacology

endothelin converting enzyme inhibitor: DT, drug therapy
endothelin converting enzyme inhibitor: PD, pharmacology
cgs 35066: DT, drug therapy
cgs 35066: PD, pharmacology
bis (7 tacrine): DT, drug therapy
bis (7 tacrine): PD, pharmacology
bis (7 tacrine): AN, drug analysis
bis (7 tacrine): DO, drug dose
conivaptan: DT, drug therapy
conivaptan: PD, pharmacology
conivaptan: CB, drug combination
conivaptan: AN, drug analysis
conivaptan: CM, drug comparison
conivaptan: DO, drug dose
carbamic acid derivative: PD, pharmacology
carbamic acid derivative: AN, drug analysis
carbamic acid derivative: DO, drug dose
carbamic acid derivative: CM, drug comparison
carbamic acid derivative: DT, drug therapy
diquafosol: PD, pharmacology
diquafosol: CM, drug comparison
diquafosol: DT, drug therapy
ns 220: DT, drug therapy
ns 220: PD, pharmacology
ns 220: CM, drug comparison
ns 220: AN, drug analysis
fenofibrate: DT, drug therapy
fenofibrate: PD, pharmacology
fenofibrate: CM, drug comparison
acetylsalicylic acid: DT, drug therapy
acetylsalicylic acid: CM, drug comparison
acetylsalicylic acid: PD, pharmacology
a 331440: DT, drug therapy
a 331440: PO, oral drug administration
a 331440: DO, drug dose
a 331440: CM, drug comparison
a 331440: PD, pharmacology
dexfenfluramine: DT, drug therapy
dexfenfluramine: CM, drug comparison
dexfenfluramine: PD, pharmacology
thioperamide: DT, drug therapy
thioperamide: CM, drug comparison
thioperamide: PD, pharmacology
ciprofloxacin: DT, drug therapy
ciprofloxacin: CM, drug comparison
ciprofloxacin: PD, pharmacology
unindexed drug
unclassified drug
ins 48372
ins 46116
ins 46117
ins 46061
ins 46058
ins 48795
ins 40150
ins 40270
ins 46060
ins 49162
ins 46059
s 35836 1

s 35678 1
gvs 111
ot 7999

RN (acetylsalicylic acid 3 (nitroxymethyl)phenyl ester) 190442-10-5; (**mitiglinide**) 145525-41-3, **207844-01-7**; (pirfenidone) 53179-13-8; (nitronaproxen) 163133-43-5; (2,4 dimethyl 5 (2 oxo 1h indol 3 ylmethylene) 3 pyrrolepropionic acid) 252916-29-3; (conivaptan) 168626-94-6, 210101-16-9; (diquafosol) 211427-08-6; (fenofibrate) 49562-28-9; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (dexfenfluramine) 3239-44-9, 3239-45-0; (thioperamide) 106243-16-7; (ciprofloxacin) 85721-33-1

CN (1) Ins 48372; (2) Ins 46116; (3) Ins 46117; (4) Ins 46061; (5) Ins 46058; (6) Ins 48795; (7) Ins 40150; (8) Ins 40270; (9) Ins 46060; (10) Ins 49162; (11) Ins 46059; (12) Ins 365; (13) Ns 220; (14) A 331440; (15) Kad 1229; (16) Kad 1229; (17) S 35836 1; (18) S 35678 1; (19) Kad 1229; (20) Gvs 111; (21) Azd 3582; (22) Azd 3582; (23) Ncx 4016; (24) Pnu 142721; (25) Su 6668; (26) Ot 7999; (27) Cgs 35066; (28) Ym 087; (29) Ym 087; (30) Amr 69; (31) Amr 69; (32) Amr 69; (33) Amr 69

CO (12) Inspire; (13) Nippon Shinyaku; (14) Abbott; (15) Kissei; (18) Servier; (19) Takeda; (20) Russian Academy of Sciences; (21) Astra Zeneca; (23) Nicox; (24) Pharmacia (United States); (25) Sugen; (26) Otsuka; (27) Novartis; (28) Yamanouchi; (29) Pfizer; (30) Marnac; (31) Intermune; (32) Schering AG; (33) Shionogi; UCB

L61 ANSWER 46 OF 49 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-08972 DRUGU T S E Full-text
TITLE: **Diabetes** and insulin resistance associated disorders: disease and the therapy.
AUTHOR: Chakrabarti R; Rajagopalan R
CORPORATE SOURCE: Dr.Reddy's-Lab.
LOCATION: Hyderabad, India
SOURCE: Curr.Sci. (83, No. 12, 1533-38, 2002) 2 Fig. 2 Tab. 18 Ref.
CODEN: CUSCAM ISSN: 0011-3891
AVAIL. OF DOC.: Dr. Reddy's Laboratories Ltd., Discovery Research, Bollaram Road, Miyapur, Hyderabad 500 050, India. (R.R.). (e-mail: rajagopalanr@drreddys.com).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

AB The therapy of **diabetes** and insulin resistance associated disorders are reviewed. Topics covered are classes of currently available drugs and future targets. Established drugs and those in trials discussed are acetohexamide, chlorpropamide, tolbutamide, tolazamide, glyburide, glipizide, glimiperide, repaglinide, nateglinide, glibenclamide, **mitiglinide**, metformin, phenformin, ciglitazone, troglitazone, rosiglitazone, pioglitazone, acarbose, miglitol (side-effects of these drugs were also mentioned), balaglitazone, natoglitazone, ragaglitazar, tesaglitazar, KRP-297, BMS-298585, regaglitazar, SR-58611, TAK-677, GP-3034, LAF-237, P-32-98, DPP-728 and NN-2211. Current research efforts are focussed on insulin sensitizers, PPAR agonists, protein tyrosine phosphatase **inhibitors**, beta-3 adrenoceptor agonists, **inhibitors** of hepatic glucose output and insulin secretagogues. (No EX).

AN 2003-08972 DRUGU T S E Full-text
T Therapeutics
S Adverse Effects
E Endocrinology
12 Antidiabetics
35 Adverse Reactions
64 Clinical Trials
69 Reviews

73 Trial Preparations
CT **DIABETES** *TR; CARBOHYDRATE-METAB.DISORDER *TR; PANCREOPATHY *TR; CASES *FT; IN-VIVO *FT; ANTIDIABETIC *FT; CLIN.TRIAL *FT; REVIEW *FT
[01] MAIN-TOPIC *FT; ANTIDIABETICS *FT; TR *FT; AE *FT
[02] ACETOHEXAMIDE *TR; CHLORPROPAMIDE *TR; TOLBUTAMIDE *TR; TOLAZAMIDE *TR; GLIBENCLAMIDE *TR; GLIPIZIDE *TR; GLIMIPERIDE *TR; REPAGLINIDE *TR; NATEGLINIDE *TR; GLIBENCLAMIDE *TR; **MITIGLINIDE** *TR; METFORMIN *TR; PHENFORMIN *TR; CIGLITAZONE *TR; TROGLITAZONE *TR; ROSIGLITAZONE *TR; PIOGLITAZONE *TR; ACARBOSE *TR; MIGLITOL *TR; BALAGLITAZONE *TR; NATOGLITAZONE *TR; RAGAGLITAZAR *TR; TESAGLITAZAR *TR; KRP-297 *TR; BMS-298585 *TR; REGAGLITAZAR *TR; SR-58611 *TR; TAK-677 *TR; GP-3034 *TR; LAF-237 *TR; P-32-98 *TR; DPP-728 *TR; NN-2211 *TR; TR *FT
[03] ACETOHEXAMIDE *AE; CHLORPROPAMIDE *AE; TOLBUTAMIDE *AE; TOLAZAMIDE *AE; GLIBENCLAMIDE *AE; GLIPIZIDE *AE; GLIMIPERIDE *AE; REPAGLINIDE *AE; NATEGLINIDE *AE; GLIBENCLAMIDE *AE; **MITIGLINIDE** *AE; METFORMIN *AE; PHENFORMIN *AE; CIGLITAZONE *AE; TROGLITAZONE *AE; ROSIGLITAZONE *AE; PIOGLITAZONE *AE; ACARBOSE *AE; MIGLITOL *AE; BALAGLITAZONE *AE; NATOGLITAZONE *AE; RAGAGLITAZAR *AE; TESAGLITAZAR *AE; KRP-297 *AE; BMS-298585 *AE; REGAGLITAZAR *AE; SR-58611 *AE; TAK-677 *AE; GP-3034 *AE; LAF-237 *AE; P-32-98 *AE; DPP-728 *AE; NN-2211 *AE; AE *FT

L61 ANSWER 47 OF 49 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-33933 DRUGU P E Full-text
TITLE: Clinical pharmacokinetics and pharmacodynamics of repaglinide.
AUTHOR: Hatorp V
LOCATION: Hoersholm, Den.
SOURCE: Clin.Pharmacokinet. (41, No. 7, 471-83, 2002) 5 Fig. 4 Tab. 48 Ref.
CODEN: CPKNDH ISSN: 0312-5963
AVAIL. OF DOC.: Danish Toxicology Center, Kogle Alle 2, DK-2970 Hoersholm, Denmark. (e-mail: vh@dtc.dk).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB Clinical pharmacokinetics and pharmacodynamics of repaglinide (RP) are reviewed. The pharmacokinetics of RP in healthy volunteers, patients with type 2 **diabetes**, and in special populations (hepatic and renal insufficiency) are analyzed. Drug-drug interactions are presented with reference to protein binding interactions and in-vivo interactions with cimetidine, digoxin, theophylline, warfarin, and rifampicin. Finally, the pharmacodynamics of RP are discussed in relation to dose tolerance, dose response and dosage regimen.
AN 2002-33933 DRUGU P E Full-text
P Pharmacology
E Endocrinology
8 Pharmacokinetics
12 Antidiabetics
66 Drug Interactions
69 Reviews
CT CASES *FT; HUMAN *FT; IN-VIVO *FT; REVIEW *FT; PHARMACOKINETICS *FT; PHARMACODYNAMICS *FT; ANTIDIABETIC *FT
[01] REPAGLINIDE *PH; REPAGLINIDE *DM; AGEE623ZW *RN; MAIN-TOPIC *FT; ANTIDIABETICS *FT; PH *FT; DM *FT
RN: 135062-02-1
[02] NATEGLINIDE *PH; **MITIGLINIDE** *PH; KETOCONAZOLE *DI;

RIFAMPICIN *DI; CIMETIDINE *DI; DIGOXIN *DI; THEOPHYLLINE *DI; WARFARIN *DI; PH *FT; DI *FT

L61 ANSWER 48 OF 49 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-11212 DRUGU P E Full-text
TITLE: Sulfonylurea stimulation of insulin secretion.
AUTHOR: Proks P; Reimann F; Green N; Gribble F; Ashcroft F
CORPORATE SOURCE: Univ.Oxford; Univ.Cambridge
LOCATION: Oxford; Cambridge, U.K.
SOURCE: Diabetes (51, Suppl. 3, S368-S376, 2002) 4 Fig. 1 Tab. 55 Ref.
CODEN: DIAEAZ ISSN: 0012-1797
AVAIL. OF DOC.: University Laboratory of Physiology, Parks Road, Oxford OX1 3PT, England. (F.A.). (e-mail: frances.ashcroft@physiol.ox.ac.uk).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB Sulfonylurea stimulation of insulin secretion is reviewed. The **inhibition** of KATP channels by imidazolines (phentolamine, cibenzoline), antimalarials (quinine, mefloquine), sulfonylureas (tolbutamide, gliclazide, glimepiride), and benzamido derivatives and the specificity of high-affinity sulfonylurea **block** are discussed. The location of the sulfonylurea binding site on SUR and interactions between Kir6.1 and SUR are explained. Modulation of sulfonylurea **block** by PIP2 and modulation of sulfonylurea **block** by MG nucleotides are considered. Findings indicate that the classification of sulfonylureas, meglitinide derivatives ect can be changed to reflect the functional differences among these drugs, and that they be referred to instead as SUR1-specific and non-SUR1-specific. (conference paper: 3rd Servier - IGIS Symposium, St. Jean Cap Ferrat, France, 2002).
AN 2003-11212 DRUGU P E Full-text
P Pharmacology
E Endocrinology
12 Antidiabetics
69 Reviews
CT REVIEW *FT; INSULIN *FT; PANCREAS-HORMONE-METAB. *FT; ANTIDIABETIC *FT; MODE-OF-ACT. *FT; IN-VIVO *FT; LAB.ANIMAL *FT
[01] MAIN-TOPIC *FT; ANTIDIABETICS *FT; PH *FT
[02] PHENTOLAMINE *PH; CIBENZOLINE *PH; QUININE *PH; MEFLOQUINE *PH; TOLBUTAMIDE *PH; GLICLAZIDE *PH; GLIMEPIRIDE *PH; MEGLITINIDE *PH; **MITIGLINIDE** *PH; NATEGLINIDE *PH; GLIBENCLAMIDE *PH; GLIPIZIDE *PH; REPAGLINIDE *PH; PH *FT

L61 ANSWER 49 OF 49 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-42236 DRUGU P T E Full-text
TITLE: Insulinotropic maglitinide analogues.
AUTHOR: Dornhorst A
CORPORATE SOURCE: Univ.London
LOCATION: London, U.K.
SOURCE: Lancet (358, No. 9294, 1709-16, 2001) 3 Fig. 78 Ref.
CODEN: LANCAO ISSN: 0140-6736
AVAIL. OF DOC.: Department of Metabolic Medicine, Faculty of Medicine, Imperial College, Hammersmith Hospital Campus, Du Cane Road, London W12 ONN, England. (e-mail: a.dornhorst@ic.ac.uk).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

AB Insulinotropic maglitinide analogs are reviewed in terms of the pathophysiology of type 2 **diabetes** and the importance of beta cell function, defects in insulin pulsatility and early-phase insulin secretion in those at risk of type 2 **diabetes.** Pharmacological approaches to type 2 **diabetes** are discussed and the mechanism of action, efficacy in clinical trials, combination therapy and pharmacokinetics, safety and tolerability of repaglinide and nateglinide are explored in detail. The ability to preserve beta cell function is compared in nateglinide and glibenclamide. **Mitiglinide** is also briefly considered along with an evaluation of recent mixed molecules such as BTS-67582. Understanding of the pathophysiology of type 2 **diabetes** is now clearer and this knowledge is beginning to yield new agents of therapeutic promise such as repaglinide and nateglinide.

AN 2001-42236 DRUGU P T E Full-text
P Pharmacology
T Therapeutics
E Endocrinology
12 Antidiabetics
64 Clinical Trials
69 Reviews

CT **DIABETES** *TR; CARBOHYDRATE-METAB.DISORDER *TR; PANCREOPATHY *TR; REVIEW *FT; IN-VITRO *FT; IN-VIVO *FT; CASES *FT; LAB.ANIMAL *FT; BETA-CELL *FT; PHARMACOKINETICS *FT; MODE-OF-ACT. *FT; INSULIN *FT; CARBOHYDRATE-METAB. *FT; CLIN.TRIAL *FT; COMB. *FT; ANTIDIABETIC *FT; PANCREAS *FT
[01] MAIN-TOPIC *FT; ANTIDIABETICS *FT; TR *FT; PH *FT
[02] MEGLITINIDE *TR; REPAGLINIDE *TR; METFORMIN *TR; TROGLITAZONE *TR; NATEGLINIDE *TR; **MITIGLINIDE** *TR; BTS-67582 *TR; S-21663 *PH; S-2166 *PH; JTT-608 *PH; MEGLITINIDE *PH; REPAGLINIDE *PH; METFORMIN *PH; TROGLITAZONE *PH; NATEGLINIDE *PH; **MITIGLINIDE** *PH; BTS-67582 *PH; GLIBENCLAMIDE *PH; TR *FT; PH *FT

******* INVENTOR RESULTS *******

```
=> d his l42

     (FILE 'HCAPLUS' ENTERED AT 14:40:20 ON 24 MAY 2007)
L42            6 S L41 NOT L33

=> d que l42
L4             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  145375-43-5/RN
L5             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  207844-01-7/RN
L6             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  MITIGLINIDE/CN
L8             2 SEA FILE=REGISTRY ABB=ON  PLU=ON  (L4 OR L5 OR L6)
L9            97 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8 OR MITIGLINIDE CALCIUM
                  HYDRATE/OBI
L10           87 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MITIGLINIDE/OBI OR MITI/OBI(W)
                  GLINIDE/OBI
L11          108 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 OR L10
L13      2160940 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (INHIBIT?/OBI OR HINDER?/OBI
                  OR IMPED?/OBI OR REDUC?/OBI OR REDN#/OBI OR SUPPRESS?/OBI OR
                  PREVENT?/OBI OR BLOCK?/OBI OR ELIMINAT?/OBI)
L19       110617 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DIABET?/OBI
L20           54 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11 AND L19
L22           28 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L13 (5A) L20
L23              QUE  ABB=ON  PLU=ON  AY<2004 OR PRY<2004 OR PY<2004 OR MY
                 <2004 OR REVIEW/DT
L24           17 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L22 AND L23
L27          271 SEA FILE=HCAPLUS ABB=ON  PLU=ON  HYPERGLYCEM?/OBI (3A)
                  (POST/OBI(W)PRANDIAL/OBI OR POSTPRANDIAL/OBI)
L28            3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11 AND L27
L29        13237 SEA FILE=HCAPLUS ABB=ON  PLU=ON  HYPERGLYCEM?/OBI
L30        13237 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L27 OR L29
L31            7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11 AND L30
L32            7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L28 OR L31
L33           24 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L32 OR L24
L34           15 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "MIKOSHIBA IMAO"/AU
L35          328 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SUZUKI HISAO/AU
L36            9 SEA FILE=HCAPLUS ABB=ON  PLU=ON  KIYONO YUJI/AU
L37          346 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L34 OR L35 OR L36)
L38          673 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("KISSEI PHARMACEUTICAL"/CO
                 OR "KISSEI PHARMACEUTICAL"/PA OR "KISSEI PHARMACEUTICAL"/CS OR
                 "KISSEI PHARMACEUTICAL CO"/CO OR "KISSEI PHARMACEUTICAL CO
                 LTD"/CO OR "KISSEI PHARMACEUTICAL CO LTD"/PA OR "KISSEI
                 PHARMACEUTICAL CO LTD"/CS OR "KISSEI PHARMACEUTICAL CO LTD
                 CENTRAL RESEARCH LABORATORIES"/CO OR "KISSEI PHARMACEUTICAL CO
                 LTD CENTRAL RESEARCH LABORATORIES HOTAKA 399 83 JAPAN"/CS OR
                 "KISSEI PHARMACEUTICAL CO LTD JAPAN"/PA OR "KISSEI PHARMACEUTIC
                 AL CO LTD JAPAN"/CS OR "KISSEI PHARMACEUTICAL CO LTD NAGANO
                 399 8304 JAPAN"/CS OR "KISSEI PHARMACEUTICAL CO LTD PHARMACEUTI
                 CAL RESEARCH LABORATORIES"/CO OR "KISSEI PHARMACEUTICAL CO LTD
                 PHARMACEUTICAL RESEARCH LABORATORIES NAGANO 399 8304 JAPAN"/CS
                 OR "KISSEI PHARMACEUTICAL CO LTD SHINSHU UNIVERSITY"/CO OR
                 "KISSEI PHARMACEUTICAL COMPANY"/CO OR "KISSEI PHARMACEUTICAL
                 COMPANY LIMITED"/CO OR "KISSEI PHARMACEUTICAL COMPANY LTD"/CO
                 OR "KISSEI PHARMACEUTICAL INDUSTRY CO LTD"/CO OR "KISSEI
                 PHARMACEUTICAL JAPAN"/PA OR "KISSEI PHARMACEUTICAL JAPAN"/CS)
L39          722 SEA FILE=HCAPLUS ABB=ON  PLU=ON  KISSEI PHARMA?/PA,CS,CO
L40          722 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L38 OR L39
L41            8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L37 AND L40
L42            6 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L41 NOT L33
```

```
=> d his l60

     (FILE 'MEDLINE, BIOSIS, EMBASE, DRUGU' ENTERED AT 14:54:53 ON 24 MAY 2007)
L60            6 S L59 NOT L49

=> d que l60
L4             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  145375-43-5/RN
L5             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  207844-01-7/RN
L6             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  MITIGLINIDE/CN
L8             2 SEA FILE=REGISTRY ABB=ON  PLU=ON  (L4 OR L5 OR L6)
L10           87 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MITIGLINIDE/OBI OR MITI/OBI(W)
                  GLINIDE/OBI
L13      2160940 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (INHIBIT?/OBI OR HINDER?/OBI
                  OR IMPED?/OBI OR REDUC?/OBI OR REDN#/OBI OR SUPPRESS?/OBI OR
                  PREVENT?/OBI OR BLOCK?/OBI OR ELIMINAT?/OBI)
L19       110617 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DIABET?/OBI
L23              QUE  ABB=ON  PLU=ON  AY<2004 OR PRY<2004 OR PY<2004 OR MY
                  <2004 OR REVIEW/DT
L27          271 SEA FILE=HCAPLUS ABB=ON  PLU=ON  HYPERGLYCEM?/OBI (3A)
                  (POST/OBI(W)PRANDIAL/OBI OR POSTPRANDIAL/OBI)
L29        13237 SEA FILE=HCAPLUS ABB=ON  PLU=ON  HYPERGLYCEM?/OBI
L43           84 SEA L8
L44          172 SEA L10
L45           10 SEA MITIGLINIDE CALCIUM HYDRATE
L46          173 SEA (L43 OR L44 OR L45)
L47          110 SEA L46 AND (L19 OR L27 OR L29)
L48           46 SEA L47 AND L23
L49           33 SEA L48 (P) L13
L50           27 SEA MIKOSHIBA I?/AU
L52           34 SEA SUZUKI HISAO/AU
L53            2 SEA KIYONO YUJI/AU
L54           63 SEA L50 OR L52 OR L53
L55            2 SEA L50 AND L52 OR L53
L56            2 SEA L54 AND L46
L57            2 SEA L55 OR L56
L58            6 SEA L54 AND (L19 OR L27 OR L29)
L59            6 SEA L57 OR L58
L60            6 SEA L59 NOT L49


=> dup rem l42 l60
PROCESSING COMPLETED FOR L42
PROCESSING COMPLETED FOR L60
L62           10 DUP REM L42 L60 (2 DUPLICATES REMOVED)
                  ANSWERS '1-6' FROM FILE HCAPLUS
                  ANSWER '7' FROM FILE MEDLINE
                  ANSWER '8' FROM FILE BIOSIS
                  ANSWER '9' FROM FILE EMBASE
                  ANSWER '10' FROM FILE DRUGU

=> d l62 1-6 ibib abs

L62  ANSWER 1 OF 10  HCAPLUS  COPYRIGHT 2007 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2004:836630  HCAPLUS  Full-text
DOCUMENT NUMBER:          142:384723
TITLE:                    Pharmacological and clinical profile of mitiglinide
                          calcium hydrate (Glufast), a new insulinotropic agent
                          with rapid onset
AUTHOR(S):                Ojima, Kazuma; Kiyono, Yuji; Kojima, Masami
```

CORPORATE SOURCE: **Pharmacol. Res. Lab. R & D, Kissei Pharm. Co., Ltd., Nagano, 399-8304, Japan**
SOURCE: Nippon Yakurigaku Zasshi (2004), 124(4), 245-255
CODEN: NYKZAU; ISSN: 0015-5691
PUBLISHER: Nippon Yakuri Gakkai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review. Mitiglinide calcium hydrate (mitiglinide, Glufast) is a new insulinotropic agent of the glinide class with rapid onset. Mitiglinide is thought to stimulate insulin secretion by closing the ATP-sensitive K+ (KATP) channels in pancreatic β-cells, and its early insulin release and short duration of action would be effective in improving postprandial hyperglycemia. In studies of various cloned KATP channels, mitiglinide shows a higher selectivity for the β-cell type of SUR1/Kir6.2 than the cardiac and smooth muscle types of KATP channels in comparison with glibenclamide and glimepiride. In vitro and in vivo studies demonstrated the insulinotropic effect of mitiglinide is more potent than that of nateglinide, and mitiglinide surpassed in controlling postprandial hyperglycemia in normal and diabetic animals. In clin. trials, treatment with mitiglinide provided lasting improvement of postprandial hyperglycemia in Type 2 diabetic patients and decreased the fasting plasma glucose levels and HbA1C values. The incidence of adverse events related to mitiglinide were nearly equivalent to placebo; in particular there was no difference with the frequency of hypoglycemia. The results from these studies indicated that mitiglinide could be expected to possess good therapeutic features of being effective in reducing postprandial glucose excursions in the early stage of Type 2 diabetes and less incidence of events suggestive of hypoglycemia.

L62 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:404898 HCAPLUS Full-text
DOCUMENT NUMBER: 146:372816
TITLE: Mitgilinide and α-glucosidase inhibitor combination for type 2 diabetes therapy
INVENTOR(S): **Kiyono, Yuji**; Okubo, Yoshio; Mototani, Katsumi; **Mikoshiba, Imao**
PATENT ASSIGNEE(S): **Kissei Pharmaceutical Co., Ltd., Japan**
SOURCE: Jpn. Kokai Tokkyo Koho, 11pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2007091641	A	20070412	JP 2005-283608	20050929
PRIORITY APPLN. INFO.:			JP 2005-283608	20050929

AB Disclosed are a pharmaceutical preparation for controlling the condition of type 2 diabetes comprising the combination of mitiglinide or a pharmacol. acceptable salt or hydrate thereof and an α-glycosidase inhibitor, e.g., voglibose. The pharmaceutical preparation shows a potent effect of decreasing the morning fasting blood glucose level, the postprandial blood glucose level and HbA1c in a patient with type 2 diabetes and can ameliorate insulin resistance.

L62 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1157536 HCAPLUS Full-text

DOCUMENT NUMBER: 145:477898
TITLE: Combined pharmaceutical preparation for treatment of type 2 diabetes
INVENTOR(S): **Kiyono, Yuji**; Okubo, Yoshio; Hontani, Katsumi; **Mikoshiba, Imao**; Ojima, Kazuma
PATENT ASSIGNEE(S): **Kissei Pharmaceutical Co., Ltd., Japan**
SOURCE: PCT Int. Appl., 29pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006115115	A1	20061102	WO 2006-JP308110	20060418

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: JP 2005-121862 A 20050420
JP 2005-166314 A 20050607

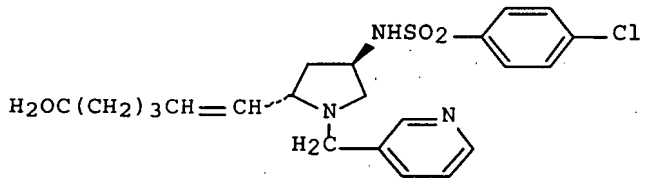
AB Disclosed are a pharmaceutical preparation for controlling the condition of type 2 diabetes, the pharmaceutical preparation comprising the combination of mitiglinide or a pharmacol. acceptable salt or hydrate thereof and an α-glycosidase inhibitor (e.g., voglibose, acarbose); and a therapeutic method using the pharmaceutical preparation The pharmaceutical preparation shows an extremely potent effect of decreasing the morning fasting blood glucose level, the postprandial blood glucose level and HbA1c in a patient with type 2 diabetes and can ameliorate glucose spike, insulin resistance and lipid metabolism

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L62 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:83073 HCAPLUS Full-text
DOCUMENT NUMBER: 124:165270
TITLE: Therapeutics for peripheral circulation disorders containing (pyridylmethyl)pyrrolidine derivative
INVENTOR(S): **Mikoshiba, Imao**; Myata, Hiroshi; Komatsu, Hidetada; Hoyano, Takeshi; Kiguchi, Sumyoshi
PATENT ASSIGNEE(S): **Kissei Pharmaceutical, Japan**
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07304671	A	19951121	JP 1994-130781	19940509

PRIORITY APPLN. INFO.: JP 1994-130781 19940509
GI



I

AB Therapeutics for symptoms caused by peripheral circulation disorders contain the title derivative (I) or its pharmacol. acceptable salts. The therapeutics are useful for treatment of rhigosis (cool sensation), numbness, and pain. I.HCl (preparation given) significantly improved neurotransmission rate in rats with streptozotocin-induced peripheral circulation disorder.

L62 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1978:115295 HCAPLUS Full-text
DOCUMENT NUMBER: 88:115295
TITLE: Effect of a combined preparation of aluminum dihydroxyallantoinate and meta-magnesium aluminosilicate (Alanta) on acute gastritis in beagles
AUTHOR(S): Azuma, Hiroshi; Shibata, Nobuo; **Mikoshiba, Imao**; Minamide, Seiki; Naito, Jun; Matsuda, Kuniaki; Kumazawa, Nariyuki
CORPORATE SOURCE: Div. **Pharmacol.**, **Kissei** Pharm. Co., Ltd., Matsumoto City, Japan
SOURCE: Oyo Yakuri (1977), 13(3), 389-98
CODEN: OYYAA2; ISSN: 0369-8033
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB The inhibitory effect of Alanta [65775-48-6] on gastritis was demonstrated by histol. examination and also by determination of fibrinolysis.

L62 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1978:99164 HCAPLUS Full-text
DOCUMENT NUMBER: 88:99164
TITLE: Pharmacological analysis of the combined effect of aluminum dihydroxyallantoinate and meta-magnesium aluminosilicate
AUTHOR(S): Azuma, Hiroshi; Naito, Jun; Tamaoki, Hiroshi; Amaki, Masaharu; **Mikoshiba, Imao**; Akahane, Masuo
CORPORATE SOURCE: Div. **Pharmacol.**, **Kissei** Pharm. Co. Ltd., Matsumoto City, Japan
SOURCE: Oyo Yakuri (1977), 13(3), 383-7
CODEN: OYYAA2; ISSN: 0369-8033
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB Aldioxa [5579-81-7] (Al dihydroxyallantoinate) dose-dependently inhibited stress-induced ulcer in rats. The ED50 of the drug was 523 mg/kg. A slight

inhibition of the stress-induced ulcer was elicited by treatment with metamagnesium aluminosilicate (MAS) [1327-43-1]. The ED50 of MAS was 25,500 mg/kg. When aldioxa and MAS were administered in combination in the ratio of 1/9, 1/19 and 1/29, the ED50 values were 1194, 1819 and 5725 mg/kg, resp. The inhibitory effect on the water immersion stress-induced ulcer was also potentiated by combined treatment with aldioxa and MAS. Aldioxa and MAS inhibited pylorus-ligation-induced ulcer in a dose-dependent manner. The ED50 values were 446 and 406 mg/kg,resp. When aldioxa and MAS were administered in the ratio of 1/9, 1/1 and 2/1, the ED50 values were 369, 395, and 405 mg/kg, resp. The inhibitory effect on pylorus-ligation ulcer induction was enhanced in an additive manner by the combined treatment.

=> d l62 7-10 ibib ab

L62 ANSWER 7 OF 10 MEDLINE on STN
ACCESSION NUMBER: 2003177108 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12694990
TITLE: Rationale and evidence for the use of oxcarbazepine in neuropathic pain.
AUTHOR: Carrazana Enrique; **Mikoshiba Imao**
CORPORATE SOURCE: Neuroscience, Clinical Development and Medical Affairs, Novartis Pharmaceuticals, East Hanover, NJ 07936-1080, USA.
SOURCE: Journal of pain and symptom management, (2003 May) Vol. 25, No. 5 Suppl, pp. S31-5. Ref: 25
Journal code: 8605836. ISSN: 0885-3924.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 17 Apr 2003
Last Updated on STN: 3 Jul 2003
Entered Medline: 2 Jul 2003

AB Oxcarbazepine is a second-generation antiepileptic drug (AED) with proven efficacy in managing partial epileptic seizures, with or without secondary generalization, in adults and children. The overlap between the underlying pathophysiologic mechanisms of some epilepsy models and neuropathic pain models supports the rationale for using certain AEDs in the treatment of neuropathic pain. Several AEDs have reportedly produced analgesia in a range of neuropathic pains, including painful **diabetic** neuropathy (PDN) and post-herpetic neuralgia. Increasing evidence suggests that oxcarbazepine can provide significant analgesia in several neuropathic pain conditions, including trigeminal neuralgia and PDN, and is also may be effective in treating neuropathic pain refractory to other AEDs, such as carbamazepine and gabapentin. The analgesic effects of oxcarbazepine, and its generally improved safety and tolerability profile compared with other standard AEDs, suggests that oxcarbazepine will be an important addition to the neuropathic pain armamentarium. The rationale and evidence to support the efficacy of oxcarbazepine are presented here.

L62 ANSWER 8 OF 10 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2000:442810 BIOSIS Full-text
DOCUMENT NUMBER: PREV200000442810
TITLE: Re-evaluation of exercise prescription for Japanese type 2 **diabetic** patients by ventilatory threshold.

AUTHOR(S): Kunitomi, Mie [Reprint author]; Takahashi, Kayo; Wada, Jun; **Suzuki, Hisao**; Miyatake, Nobuyuki; Ogawa, Saeko; Ohta, Sachiko; Sugimoto, Hikaru; Shikata, Kenichi; Makino, Hirofumi

CORPORATE SOURCE: Department of Medicine III, Okayama University Medical School, 2-5-1 Shikata-cho, Okayama, 700-8558, Japan

SOURCE: Diabetes Research and Clinical Practice, (October, 2000) Vol. 50, No. 2, pp. 109-115. print.
CODEN: DRCPE9. ISSN: 0168-8227.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 18 Oct 2000
Last Updated on STN: 10 Jan 2002

AB Prescription of aerobic exercise for Type 2 **diabetes** mellitus (Type 2 DM) in clinical practice is frequently based on exercise intensity at maximum heart rate (60 < HRmax < 79%), heart rate reserve (50 < HRreserve < 74%), and rating of perceived exertion (12 < RPE < 13). We examined these parameters in Japanese males with Type 2 DM at ventilatory threshold (VT) to investigate the exercise capacity of Type 2 DM patients and re-evaluate the exercise prescription. Fifty-six Japanese Type 2 DM males without autonomic neuropathy (age, 53.5 +- 7.7 years; body mass index (BMI), 23.7 +- 3.6 kg/m2) were enrolled and compared with 56 age- and BMI-matched healthy Japanese males. VT was determined breath by breath during exercise test using a ramp protocol and rates of oxygen consumption (VO2), work rate (WR), HR, DELTAHR, %HRmax, %HRreserve, and RPE were measured at VT. Type 2 DM patients had significantly lower VO2 (3.6 +- 0.4 metabolic equivalents (METs)) and WR (62 +- 14 W) than controls (VO2, 3.9 +- 0.6 METs; WR, 74 +- 13 W). %HRreserve, (32.6 +- 7.7%) was also significantly lower compared with controls (37.6 +- 8.3%), while %HRmax, was not different. RPE was also similar in **diabetics** (12.4 +- 1.5) and controls (12.9 +- 1.2), however, it was significantly lower in **diabetic** patients aged 60-69 years (11.8 +- 2.0) and those with distal symmetric sensory neuropathy (12.2 +- 1.0). Our results indicate reduced exercise capacity in Japanese Type 2 DM males and the exercise intensity of 60%HRmax, 30%HRreserve, and RPE 12 is recommended in elderly **diabetics** and those with **diabetic** sensory neuropathy.

L62 ANSWER 9 OF 10 EMBASE

ACCESSION NUMBER: 2003151062 EMBASE Full-text

TITLE: Rationale and evidence for the use of oxcarbazepine in neuropathic pain.

AUTHOR: Carrazana E.; **Mikoshiba I.**

CORPORATE SOURCE: Dr. E. Carrazana, Neurosci., Clin. Devmt./Med. Affairs, Novartis Pharmaceuticals, Building 403, 59 Route 10, East Hanover, NJ 07936-1080, United States

SOURCE: Journal of Pain and Symptom Management, (1 May 2003) Vol. 25, No. 5 SUPPL., pp. S31-S35. .
Refs: 25
ISSN: 0885-3924 CODEN: JPSMEU

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 003 Endocrinology
008 Neurology and Neurosurgery
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 24 Apr 2003
Last Updated on STN: 24 Apr 2003

AB Oxcarbazepine is a second-generation antiepileptic drug (AED) with proven efficacy in managing partial epileptic seizures, with or without secondary generalization, in adults and children. The overlap between the underlying pathophysiologic mechanisms of some epilepsy models and neuropathic pain models supports the rationale for using certain AEDs in the treatment of neuropathic pain. Several AEDs have reportedly produced analgesia in a range of neuropathic pains, including painful **diabetic** neuropathy (PDN) and post-herpetic neuralgia. Increasing evidence suggests that oxcarbazepine can provide significant analgesia in several neuropathic pain conditions, including trigeminal neuralgia and PDN, and is also may be effective in treating neuropathic pain refractory to other AEDs, such as carbamazepine and gabapentin. The analgesic effects of oxcarbazepine, and its generally improved safety and tolerability profile compared with other standard AEDs, suggests that oxcarbazepine will be an important addition to the neuropathic pain armamentarium. The rationale and evidence to support the efficacy of oxcarbazepine are presented here.

L62 ANSWER 10 OF 10 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-26991 DRUGU T S Full-text
TITLE: Neuropathic pain: from mechanisms to treatment strategies. Rationale and evidence for the use of oxcarbazepine in neuropathic pain.
AUTHOR: Carrazana E; **Mikoshiba I**
CORPORATE SOURCE: Novartis; Kissei
LOCATION: East Hanover, N.J., USA; Tokyo, Jap.
SOURCE: J.Pain Symptom Manage. (25, No. 5, Suppl., S31-S35, 2003) 1 Fig. 1 Tab. 25 Ref.
CODEN: JPSMEU ISSN: 0885-3924
AVAIL. OF DOC.: Neuroscience, Clinical Development and Medical Affairs, Novartis Pharmaceuticals, Building 403, Room 362, 59 Route 10, East Hanover, NJ, 07936-1080, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

AB The use of oxcarbazepine in neuropathic pain is reviewed. Oxcarbazepine as a treatment for neuropathic pain including clinical evidence in trigeminal neuralgia, other neuropathic pain conditions and painful **diabetic** neuropathy are discussed. Oxcarbazepine is an effective and well tolerated treatment for neuropathic pain. This efficacy has been noted in a broad range of neuropathic pain conditions, including trigeminal neuralgia and painful **diabetic** neuropathy, and in patients refractory to other antiepileptic drugs, such as carbamazepine and gabapentin.

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=> d his nofile

     (FILE 'HOME' ENTERED AT 14:30:01 ON 24 MAY 2007)

     FILE 'HCAPLUS' ENTERED AT 14:31:22 ON 24 MAY 2007
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                 D ALL
L3             2 SEA ABB=ON  PLU=ON  L1 OR L2

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L5             1 SEA ABB=ON  PLU=ON  207844-01-7/RN
L6             1 SEA ABB=ON  PLU=ON  MITIGLINIDE/CN
L7             0 SEA ABB=ON  PLU=ON  MITIGLINIDE CALCIUM HYDRATE/CN
L8             2 SEA ABB=ON  PLU=ON  (L4 OR L5 OR L6)

     FILE 'HCAPLUS' ENTERED AT 14:35:34 ON 24 MAY 2007
L9            97 SEA ABB=ON  PLU=ON  L8 OR MITIGLINIDE CALCIUM HYDRATE/OBI
L10           87 SEA ABB=ON  PLU=ON  MITIGLINIDE/OBI OR MITI/OBI(W)GLINIDE/OBI
L11          108 SEA ABB=ON  PLU=ON  L9 OR L10
L12         3944 SEA ABB=ON  PLU=ON  DIABET?/OBI (L) (PROGRESS?/OBI OR COMPLICAT
                 ?/OBI)
L13      2160940 SEA ABB=ON  PLU=ON  (INHIBIT?/OBI OR HINDER?/OBI OR IMPED?/OBI
                 OR REDUC?/OBI OR REDN#/OBI OR SUPPRESS?/OBI OR PREVENT?/OBI OR
                 BLOCK?/OBI OR ELIMINAT?/OBI)
L14         1486 SEA ABB=ON  PLU=ON  L12 AND L13
L15         1486 SEA ABB=ON  PLU=ON  L12 (P) L13
L16            3 SEA ABB=ON  PLU=ON  L10 AND L15
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     FILE 'STNGUIDE' ENTERED AT 14:39:04 ON 24 MAY 2007

     FILE 'HCAPLUS' ENTERED AT 14:40:20 ON 24 MAY 2007
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L18            0 SEA ABB=ON  PLU=ON  L17 NOT L16
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L19       110617 SEA ABB=ON  PLU=ON  DIABET?/OBI
L20           54 SEA ABB=ON  PLU=ON  L11 AND L19
L21           28 SEA ABB=ON  PLU=ON  L13 AND L20
L22           28 SEA ABB=ON  PLU=ON  L13 (5A) L20
                 D KWIC 1-5
                 D L22 TI 1-5
L23              QUE ABB=ON  PLU=ON  AY<2004 OR PRY<2004 OR PY<2004 OR MY<2004
                 OR REVIEW/DT
L24           17 SEA ABB=ON  PLU=ON  L22 AND L23
L25            3 SEA ABB=ON  PLU=ON  L10 AND L12
L26           17 SEA ABB=ON  PLU=ON  L24 OR L25
L27          271 SEA ABB=ON  PLU=ON  HYPERGLYCEM?/OBI (3A) (POST/OBI(W)PRANDIAL/
                 OBI OR POSTPRANDIAL/OBI)
L28            3 SEA ABB=ON  PLU=ON  L11 AND L27
                 D TI 1-3
L29        13237 SEA ABB=ON  PLU=ON  HYPERGLYCEM?/OBI
L30        13237 SEA ABB=ON  PLU=ON  L27 OR L29
L31            7 SEA ABB=ON  PLU=ON  L11 AND L30
L32            7 SEA ABB=ON  PLU=ON  L28 OR L31
L33           24 SEA ABB=ON  PLU=ON  L32 OR L24
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L36           9 SEA ABB=ON  PLU=ON  KIYONO YUJI/AU
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                PHARMACEUTICAL"/PA OR "KISSEI PHARMACEUTICAL"/CS OR "KISSEI
                PHARMACEUTICAL CO"/CO OR "KISSEI PHARMACEUTICAL CO LTD"/CO OR
                "KISSEI PHARMACEUTICAL CO LTD"/PA OR "KISSEI PHARMACEUTICAL CO
                LTD"/CS OR "KISSEI PHARMACEUTICAL CO LTD CENTRAL RESEARCH
                LABORATORIES"/CO OR "KISSEI PHARMACEUTICAL CO LTD CENTRAL
                RESEARCH LABORATORIES HOTAKA 399 83 JAPAN"/CS OR "KISSEI
                PHARMACEUTICAL CO LTD JAPAN"/PA OR "KISSEI PHARMACEUTICAL CO
                LTD JAPAN"/CS OR "KISSEI PHARMACEUTICAL CO LTD NAGANO 399 8304
                JAPAN"/CS OR "KISSEI PHARMACEUTICAL CO LTD PHARMACEUTICAL
                RESEARCH LABORATORIES"/CO OR "KISSEI PHARMACEUTICAL CO LTD
                PHARMACEUTICAL RESEARCH LABORATORIES NAGANO 399 8304 JAPAN"/CS
                OR "KISSEI PHARMACEUTICAL CO LTD SHINSHU UNIVERSITY"/CO OR
                "KISSEI PHARMACEUTICAL COMPANY"/CO OR "KISSEI PHARMACEUTICAL
                COMPANY LIMITED"/CO OR "KISSEI PHARMACEUTICAL COMPANY LTD"/CO
                OR "KISSEI PHARMACEUTICAL INDUSTRY CO LTD"/CO OR "KISSEI
                PHARMACEUTICAL JAPAN"/PA OR "KISSEI PHARMACEUTICAL JAPAN"/CS)
L39         722 SEA ABB=ON  PLU=ON  KISSEI PHARMA?/PA,CS,CO
L40         722 SEA ABB=ON  PLU=ON  L38 OR L39
L41           8 SEA ABB=ON  PLU=ON  L37 AND L40
L42           6 SEA ABB=ON  PLU=ON  L41 NOT L33
                SAVE TEMP L42 FIN155HCAAU/A

    FILE 'MEDLINE, BIOSIS, EMBASE, DRUGU' ENTERED AT 14:54:53 ON 24 MAY 2007
L43          84 SEA ABB=ON  PLU=ON  L8
L44         172 SEA ABB=ON  PLU=ON  L10
L45          10 SEA ABB=ON  PLU=ON  MITIGLINIDE CALCIUM HYDRATE
L46         173 SEA ABB=ON  PLU=ON  (L43 OR L44 OR L45)
L47         110 SEA ABB=ON  PLU=ON  L46 AND (L19 OR L27 OR L29)
L48          46 SEA ABB=ON  PLU=ON  L47 AND L23
L49          33 SEA ABB=ON  PLU=ON  L48 (P) L13
                D TRIAL 1-5
                SAVE TEMP L49 FIN155MULTI/A
L50          27 SEA ABB=ON  PLU=ON  MIKOSHIBA I?/AU
L51       22092 SEA ABB=ON  PLU=ON  SUZUKI H?/AU
L52          34 SEA ABB=ON  PLU=ON  SUZUKI HISAO/AU
L53           2 SEA ABB=ON  PLU=ON  KIYONO YUJI/AU
L54          63 SEA ABB=ON  PLU=ON  L50 OR L52 OR L53
L55           2 SEA ABB=ON  PLU=ON  L50 AND L52 OR L53
L56           2 SEA ABB=ON  PLU=ON  L54 AND L46
L57           2 SEA ABB=ON  PLU=ON  L55 OR L56
L58           6 SEA ABB=ON  PLU=ON  L54 AND (L19 OR L27 OR L29)
L59           6 SEA ABB=ON  PLU=ON  L57 OR L58
                D L59 TI 1-6
L60           6 SEA ABB=ON  PLU=ON  L59 NOT L49
                SAVE TEMP L60 FIN155MULAU/A

    FILE 'STNGUIDE' ENTERED AT 15:06:18 ON 24 MAY 2007
                D QUE L33
                D QUE L49
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     FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, DRUGU' ENTERED AT 15:07:58 ON 24
     MAY 2007
L61          49 DUP REM L33 L49 (8 DUPLICATES REMOVED)
                   ANSWERS '1-24' FROM FILE HCAPLUS
                   ANSWERS '25-42' FROM FILE MEDLINE
                   ANSWERS '43-45' FROM FILE EMBASE
                   ANSWERS '46-49' FROM FILE DRUGU
               D L61 1-24 IBIB ED ABS HITIND
               D L61 25-49 IBIB AB IND
               D QUE L42
               D QUE L60
L62          10 DUP REM L42 L60 (2 DUPLICATES REMOVED)
                   ANSWERS '1-6' FROM FILE HCAPLUS
                   ANSWER '7' FROM FILE MEDLINE
                   ANSWER '8' FROM FILE BIOSIS
                   ANSWER '9' FROM FILE EMBASE
                   ANSWER '10' FROM FILE DRUGU
               D L62 1-6 IBIB ABS
               D L62 7-10 IBIB AB
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ANSWER SUMMARY

L2 ANSWER 1 OF 1416 CAPLUS

Voltage regulator [machine translation]; 2007:536206 CAPLUS

L2 ANSWER 2 OF 1416 CAPLUS

An optical drive having a laser driver device with an adjustable power level; 2007:512519 CAPLUS

L2 ANSWER 3 OF 1416 CAPLUS

PCR detection of Reg IV mRNA for cancer diagnosis; 2007:485237 CAPLUS

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2-Propenoic acid, methyl ester, polymer with ethenyl acetate, hydrolyzed, sodium salts; tolerance exemption; 2007:473041 CAPLUS

L2 ANSWER 5 OF 1416 CAPLUS

Roles of CD4+CD25+ T cells in the development of experimental murine allergic conjunctivitis; 2007:471425 CAPLUS

L1 ANSWER 1 OF 90 CAPLUS

Combinations of metformin and meglitinide; 2007:537722 CAPLUS

L3 ANSWER 1 OF 4 REGISTRY

(αS,3aR,7aS)- octahydro-γ-oxo-α-(phenylmethyl)-2H-Isoindole-2-butanoic acid, calcium salt (2:1); 145525-41-3 REGISTRY

L3 ANSWER 1 OF 4 REGISTRY

(αS,3aR,7aS)- octahydro-γ-oxo-α-(phenylmethyl)-2H-Isoindole-2-butanoic acid, calcium salt (2:1); 145525-41-3 REGISTRY

L3 ANSWER 2 OF 4 REGISTRY

(αS,3aR,7aS)- octahydro-γ-oxo-α-(phenylmethyl)-2H-Isoindole-2-butanoic acid; 145375-43-5 REGISTRY

L3 ANSWER 3 OF 4 REGISTRY

hydrochloride (1:2) 4-[3-[2-(trifluoromethyl)-10H-phenothiazin-10-yl]propyl]-1-Piperazineethanol; 146-56-5 REGISTRY

L3 ANSWER 4 OF 4 REGISTRY

4-chloro-α-(4-chlorophenyl)-α-(trichloromethyl)- Benzenemethanol; 115-32-2 REGISTRY

L7 ANSWER 1 OF 85 CAPLUS

Combinations of metformin and meglitinide; 2007:537722 CAPLUS

L7 ANSWER 2 OF 85 CAPLUS

Carboxyl-glucuronidation of mitiglinide by human UDP-glucuronosyltransferases; 2007:453224 CAPLUS

L7 ANSWER 3 OF 85 CAPLUS

Mitgilinide and α-glucosidase inhibitor combination for type 2 diabetes therapy; 2007:404898 CAPLUS

L7 ANSWER 4 OF 85 CAPLUS

Combination therapy for controlled carbohydrate digestion, decreased formation of intestinal gas, and modulation of insulin signaling or blood glucose levels; 2007:329618 CAPLUS

L7 ANSWER 5 OF 85 CAPLUS

Administration of dipeptidyl peptidase inhibitors; 2007:287177 CAPLUS

L4 ANSWER 1 OF 6 CAPLUS

Characterization of the action of S 21403 (mitiglinide) on insulin secretion and biosynthesis in normal and diabetic β-cells; 2005:1205798 CAPLUS

L4 ANSWER 2 OF 6 CAPLUS
Pharmacological and clinical profile of mitiglinide calcium hydrate (Glufast), a new insulinotropic agent with rapid onset; 2004:836630 CAPLUS

L4 ANSWER 3 OF 6 CAPLUS

Rapid-onset hypoglycemic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostprandial-hyperglycemia agent. comparison with glimepiride; 2004:496322 CAPLUS

L4 ANSWER 4 OF 6 CAPLUS

Rapid onset-insulinotropic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostpradial hyperglycemic agent: comparison with nateglinide; 2004:345396 CAPLUS

L4 ANSWER 5 OF 6 CAPLUS

Characterization of hypoglycemic effect of mitiglinide calcium dihydrate (KAD-1229), a novel hypoglycemic agent: comparison with glibenclamide, a sulfonylurea; 2004:345395 CAPLUS

L4 ANSWER 6 OF 6 CAPLUS

Effects of S 21403 on hormone secretion from isolated rat pancreas at different glucose concentrations; 2002:894053 CAPLUS

L1 ANSWER 1 OF 2 REGISTRY

(αS,3aR,7aS)- octahydro-γ-oxo-α-(phenylmethyl)-2H-Isoindole-2-butanoic acid, calcium salt (2:1); 145525-41-3 REGISTRY

L3 ANSWER 1 OF 129 CAPLUS

Combinations of metformin and meglitinide; 2007:537722 CAPLUS

L3 ANSWER 2 OF 129 CAPLUS

Mitgilinide and α-glucosidase inhibitor combination for type 2 diabetes therapy; 2007:404898 CAPLUS

L3 ANSWER 3 OF 129 CAPLUS

Combination therapy for controlled carbohydrate digestion, decreased formation of intestinal gas, and modulation of insulin signaling or blood glucose levels; 2007:329618 CAPLUS

L3 ANSWER 4 OF 129 CAPLUS

Administration of dipeptidyl peptidase inhibitors; 2007:287177 CAPLUS

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L3 ANSWER 6 OF 129 CAPLUS

Study on environmental risk assessment of drugs: excretion forms to environment; 2007:276713 CAPLUS

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High-performance liquid chromatography-electrospray ionization mass spectrometry determination of Mitiglinide in human plasma and its pharmacokinetics; 2007:207390 CAPLUS

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Sulfonylureas and glinides exhibit peroxisome proliferator-activated receptor γ activity: a combined virtual screening and biological assay approach; 2007:141807 CAPLUS

L3 ANSWER 9 OF 129 CAPLUS

Potassium channel blockers for treatment of migraine and headache; 2007:88262 CAPLUS

L3 ANSWER 10 OF 129 CAPLUS

Preparation of N-terminally modified GLP-1 receptor modulators and their use in the

treatment of diabetes and related conditions; 2006:1253322 CAPLUS

L5 ANSWER 1 OF 91 CAPLUS

Long-term effect of combination therapy with mitiglinide and once daily insulin glargine in patients who were successfully switched from intensive insulin therapy in short-term study; 2007:548465 CAPLUS

L5 ANSWER 2 OF 91 CAPLUS

Combinations of metformin and meglitinide; 2007:537722 CAPLUS

L5 ANSWER 3 OF 91 CAPLUS

Carboxyl-glucuronidation of mitiglinide by human UDP-glucuronosyltransferases; 2007:453224 CAPLUS

L5 ANSWER 4 OF 91 CAPLUS

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L5 ANSWER 5 OF 91 CAPLUS

Combination therapy for controlled carbohydrate digestion, decreased formation of intestinal gas, and modulation of insulin signaling or blood glucose levels; 2007:329618 CAPLUS

L5 ANSWER 6 OF 91 CAPLUS

Administration of dipeptidyl peptidase inhibitors; 2007:287177 CAPLUS

L5 ANSWER 7 OF 91 CAPLUS

Administration of dipeptidyl peptidase inhibitors; 2007:287142 CAPLUS

L5 ANSWER 8 OF 91 CAPLUS

Sulfonylureas and glinides exhibit peroxisome proliferator-activated receptor γ activity: a combined virtual screening and biological assay approach; 2007:141807 CAPLUS

L5 ANSWER 9 OF 91 CAPLUS

Preparation of N-terminally modified GLP-1 receptor modulators and their use in the treatment of diabetes and related conditions; 2006:1253322 CAPLUS

L5 ANSWER 10 OF 91 CAPLUS

Preparation of pyrazole compounds as hepatic glycogen phosphorylase inhibitors and therapeutic agents for diabetes; 2006:1252442 CAPLUS

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Combined pharmaceutical preparation for treatment of type 2 diabetes; 2006:1157536 CAPLUS

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Imaging docking and fusion of insulin granules induced by antidiabetes agents. Sulfonylurea and glinide drugs preferentially mediate the fusion of newcomer, but not previously docked, insulin granules; 2006:1056090 CAPLUS

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Process for preparation of isoindoline derivatives as antidiabetic agents; 2006:969655 CAPLUS

L5 ANSWER 14 OF 91 CAPLUS

Roflumilast for the treatment of diabetes mellitus; 2006:945768 CAPLUS

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Roflumilast for the treatment of diabetes mellitus and accompanying disorders, and combinations with other agents; 2006:944442 CAPLUS

L5 ANSWER 16 OF 91 CAPLUS

Effects of mitiglinide on glucose -induced insulin release into the portal vein and fat-induced triglyceride elevation in prediabetic and diabetic OLETF rats. [Erratum to document cited in CA145:262963]; 2006:898535 CAPLUS

L5 ANSWER 17 OF 91 CAPLUS

Manufacture and application of drug composition containing pioglitazone hydrochloride and mitiglinide for treating insulin-dependent diabetes mellitus; 2006:840773 CAPLUS

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Manufacture of dripping pill containing mitiglinide for treating diabetes mellitus; 2006:840772 CAPLUS

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Medicinal compositions containing hypoglycemic agents; 2006:766544 CAPLUS

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Manufacture of mitiglinide enteric-coated preparation; 2006:666684 CAPLUS

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Effects of mitiglinide on glucose -induced insulin release into the portal vein and fat-induced triglyceride elevation in prediabetic and diabetic OLETF rats; 2006:664881 CAPLUS

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Mitiglinide sustained-release preparation and its production method; 2006:519723 CAPLUS

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Therapeutic efficacy of mitiglinide combined with once daily insulin glargine after switching from multiple daily insulin regimen of aspart insulin and glargine in patients with type 2 diabetes mellitus; 2006:505268 CAPLUS

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Synthesis and hypoglycemic activity of mitiglinide analogs; 2006:328612 CAPLUS

L5 ANSWER 25 OF 91 CAPLUS

Mitiglinide oral preparations for the treatment of diabetes; 2006:220560 CAPLUS

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Rapid insulin secretagogue: Mitiglinide; 2006:64372 CAPLUS

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Manufacture of compound hypoglycemic drug containing mitiglinide and metformin hydrochloride; 2006:39395 CAPLUS

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Pharmaceutical composition for prevention or treatment of lipid metabolism disorder; 2005:1220708 CAPLUS

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Characterization of the action of S 21403 (mitiglinide) on insulin secretion and biosynthesis in normal and diabetic β-cells; 2005:1205798 CAPLUS

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Effects of S21403 (mitiglinide) on postprandial generation of oxidative stress and inflammation in type 2 diabetic patients; 2005:1009580 CAPLUS

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Method for examining blood glucose control state; 2005:962511 CAPLUS

L5 ANSWER 32 OF 91 CAPLUS

Preparation of 5-substituted 2H-pyrazole-3-carboxylic acid derivatives as agonists for the RUP25 nicotinic acid receptor for the treatment of dyslipidemia and related diseases; 2005:120729 CAPLUS

L5 ANSWER 33 OF 91 CAPLUS
Rapid acting insulin secretagogue in treatment for type 2 diabetes; 2005:43407 CAPLUS

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The impact of ATP-sensitive K+ channel subtype selectivity of insulin secretagogues for the coronary vasculature and the myocardium; 2004:1076146 CAPLUS

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Mitiglinide calcium dihydrate; 2004:1072015 CAPLUS

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Synthesis of antidiabetic mitiglinide calcium hydrate; 2004:1070406 CAPLUS

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A synergistic pharmaceutical combination comprising cicletanine for the prevention or treatment of diabetes; 2004:902180 CAPLUS

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Pharmacological and clinical profile of mitiglinide calcium hydrate (Glufast), a new insulinotropic agent with rapid onset; 2004:836630 CAPLUS

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Remedy for diabetes; 2004:681582 CAPLUS

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Rapid-onset hypoglycemic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostprandial-hyperglycemia agent. comparison with glimepiride; 2004:496322 CAPLUS

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Rapid onset-insulinotropic effect of mitiglinide calcium dihydrate (KAD-1229), a novel antipostpradial hyperglycemic agent: comparison with nateglinide; 2004:345396 CAPLUS

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Characterization of hypoglycemic effect of mitiglinide calcium dihydrate (KAD-1229), a novel hypoglycemic agent: comparison with glibenclamide, a sulfonylurea; 2004:345395 CAPLUS

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Preparation of aroylhydroxypyrazoles for treatment of metabolic disorders; 2004:333698 CAPLUS

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Cardiovascular risk in type 2 diabetics and pharmacological regulation of mealtime glucose excursions; 2004:202949 CAPLUS

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Bicyclic oligopeptides and their use as glucagon receptor antagonists; 2004:60541 CAPLUS

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Bicyclic oligopeptides and their use as glucagon receptor antagonists; 2004:60532 CAPLUS

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Drug composition for prevention or inhibition of advance of diabetic complication; 2004:20487 CAPLUS

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Drug composition for blood sugar control; 2004:20486 CAPLUS

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Antidiabetic preparation for oral administration; 2004:3671 CAPLUS

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Pharmacology of the meglitinide analogs: new treatment options for type 2 diabetes mellitus; 2003:1000347 CAPLUS

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Therapeutic agent for diabetes; 2003:931184 CAPLUS

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Uptake of tritiated mitiglinide by pancreatic pieces and islets; 2003:780556 CAPLUS

L5 ANSWER 53 OF 91 CAPLUS

Combination of a HMG-CoA reductase inhibitor and an insulin secretion enhancer; 2003:777602 CAPLUS

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Oral pharmaceutical composition containing mitiglinide; 2003:573217 CAPLUS

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Use of an immediate-release powder in pharmaceutical and nutraceutical compositions; 2003:511859 CAPLUS

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Pharmaceutical compositions containing a renin inhibitor and antidiabetics; 2003:473243 CAPLUS

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Synergistic antidiabetic combinations containing antihyperlipemics and hydroximic acids; 2003:76614 CAPLUS

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Effects of S 21403 on hormone secretion from isolated rat pancreas at different glucose concentrations; 2002:894053 CAPLUS

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Processes for preparation of optically active 2-benzylsuccinic acid and optically active 2-benzylsuccinic acid monoamides; 2002:832745 CAPLUS

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Study of the insulinotropic effect of the novel antihyperglycemic agent KAD-1229 using HIT T15 cells, a hamster's insulinoma cell line; 2002:743481 CAPLUS

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Compositions comprising a polypeptide and an active agent; 2002:556104 CAPLUS

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Effect of KAD-1229, a novel hypoglycaemic agent, on plasma glucose levels after meal load in type 2 diabetic rats; 2002:395747 CAPLUS

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Compositions comprising a polypeptide and an active agent; 2002:332011 CAPLUS

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Drugs for diabetes, especially type 2, comprising an antiinflammatory or analgesic drug, selected bivalent linkers, and a nitrate ester; 2002:293592 CAPLUS

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Pharmaceutical compositions containing AT-receptor antagonist or insulin secretion enhancers; 2002:157602 CAPLUS

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Combinations of insulin secretion enhancer, HMG-CoA reductase inhibitors and acetylcholinesterase inhibitors; 2002:157564 CAPLUS

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A combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for the treatment of diabetes; 2002:51257 CAPLUS

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Absence of exacerbation of myocardial stunning in anesthetized dogs treated with KAD-1229, a novel hypoglycemic agent; 2001:864540 CAPLUS

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The effects of mitiglinide (KAD-1229), a new antidiabetic drug, on ATP-sensitive K+ channels and insulin secretion: comparison with the sulfonylureas and nateglinide; 2001:857058 CAPLUS

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Antidiabetic agents containing α-glucosidase inhibitors and insulin secretion promoters; 2001:635931 CAPLUS

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Rapid acting insulinotropic agents: restoration of early insulin secretion as a physiologic approach to improve glucose control; 2001:620286 CAPLUS

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Effects of mitiglinide (s 21403) on Kir6.2/SUR1, Kir6.2/SUR2A and Kir6.2/SUR2B types of ATP-sensitive potassium channel; 2001:282226 CAPLUS

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Effect of KAD-1229, a nonsulfonylurea hypoglycemic agent, on plasma glucose and insulin in streptozotocin-induced diabetic dogs; 2001:166771 CAPLUS

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Immediate-release oral pharmaceutical compositions containing benzylsuccinate derivatives; 2000:841976 CAPLUS

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Use of succinic acid derivatives to obtain a medicine for treating inflammation; 2000:814308 CAPLUS

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Recent developments and emerging therapies for type 2 diabetes mellitus; 2000:194936 CAPLUS

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Antidiabetic oral formulations containing benzylsuccinic acid derivative; 2000:59962 CAPLUS

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Effect of the Meglitinide analog S21403 on cationic fluxes and insulin release in perfused rat pancreatic islets exposed to a high concentration od D- Glucose; 1999:573477 CAPLUS

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Process for producing benzylsuccinic acid derivatives; 1998:527315 CAPLUS

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Process for producing optically active benzylsuccinic acid by optical resolution; 1998:527305 CAPLUS

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Effect of a novel hypoglycemic agent, KAD-1229 on glucose metabolism and fructose-2, 6- bisphosphate content in isolated hepatocytes of normal rats; 1996:730982 CAPLUS

L5 ANSWER 82 OF 91 CAPLUS

Effect of the meglitinide analog KAD-1229 on 45Ca outflow and insulin release in

pancreatic islets; 1996:647356 CAPLUS

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Effects of the methyl esters of pyruvate, succinate and glutamate on the secretory response to meglitinide analogs in rat pancreatic islets; 1996:584776 CAPLUS

L5 ANSWER 84 OF 91 CAPLUS

A rapid- and short-acting hypoglycemic agent KAD-1229 improves post-prandial hyperglycemia and diabetic complications in streptozotocin-induced non-insulin-dependent diabetes mellitus rats; 1996:536607 CAPLUS

L5 ANSWER 85 OF 91 CAPLUS

Effect of a non-sulfonylurea hypoglycemic agent, KAD-1229 on hormone secretion in the isolated perfused pancreas of the rat; 1996:269911 CAPLUS

L5 ANSWER 86 OF 91 CAPLUS

Insulinotropic action of meglitinide analogs: modulation by an activator of ATP-sensitive K+ channels and high extracellular K+ concentrations; 1996:156362 CAPLUS

L5 ANSWER 87 OF 91 CAPLUS

Insulinotropic action of (2S)-2-benzyl-3-(cis- hexahydro-2-isoindolinylcarbonyl) propionate I. Secretory and cationic aspects; 1995:747679 CAPLUS

L5 ANSWER 88 OF 91 CAPLUS

Normalization of impaired glucose tolerance by the short-acting hypoglycemic agent calcium (2S)-2-benzyl-3-(cis-hexahydro-2- isoindolinylcarbonyl)propionate dihydrate (KAD-1229) in non-insulin-dependent diabetes mellitus rats; 1995:477544 CAPLUS

L5 ANSWER 89 OF 91 CAPLUS

Inhibition of ATP-sensitive K+ channel by a non-sulfonylurea compound KAD-1229 in a pancreatic β-cell line, MIN 6 cell; 1995:231935 CAPLUS

L5 ANSWER 90 OF 91 CAPLUS

Novel rapid- and short-acting hypoglycemic agent, a calcium(2s)- 2-benzyl-3-(cis-hexahydro-2- isoindolinylcarbonyl)propionate (KAD-1229) that acts on the sulfonylurea receptor: comparison of effects between KAD-1229 and gliclazide; 1994:426648 CAPLUS

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Preparation of succinic acid azabicyclylamides and related compounds as antidiabetics; 1993:59584 CAPLUS

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